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ORGANIC SYNTHESES

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ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY
METHODS FOR THE PREPARATION
OF ORGANIC CHEMICALS

Volume 33

1953

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NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

SUBMISSION OF PREPARATIONS

Chemists are invited to submit for publication in *Organic Syntheses* procedures for the preparation of compounds which are of general interest or which illustrate useful synthetic methods. The procedures submitted should represent, as nearly as possible, optimum conditions for the preparations, and should have been checked carefully by the submitter. Full details of all steps in the procedure should be included, and the range of yields should be reported rather than the maximum yield obtainable. The melting point of each solid product should be given, and the boiling-point range and refractive index (at 25°) of each liquid product. The method of preparation or source of the reactants and the criteria for the purity of the products should be stated.

Procedures submitted should be written in the style employed in the latest volume of *Organic Syntheses*. Copies of the current style sheet may be obtained upon request from the Secretary of the Editorial Board. Two copies of procedures which are submitted should be sent to the Secretary. Additions, corrections, and improvements to preparations previously published are welcomed and should be sent to the Secretary.

3-ACETAMIDO-2-BUTANONE

(2-Butanone, 3-acetamido-)

$$CH_3CH(NH_2)CO_2H + 2(CH_3CO)_2O \xrightarrow{\text{Pyridine}} CH_3CH(NHCOCH_3)COCH_3 + CO_2 + 2CH_3CO_2H$$

Submitted by Richard H. Wiley and O. H. Borum.[1]
Checked by R. S. Schreiber and B. D. Aspergren.

1. Procedure

A mixture of 156.6 g. (159 ml., 1.98 moles) of pyridine (Note 1), 239.9 g. (224 ml., 2.35 moles) of acetic anhydride (Note 2), and 35.1 g. (0.394 mole) of vacuum-dried alanine (Notes 3 and 4) is heated with stirring (Note 5) on the steam bath for 6 hours after solution is complete (Note 6). The excess pyridine and acetic anhydride, and the acetic acid, are removed at reduced pressure. The residue is distilled through a 15-cm. column, packed with glass helices, to give 41.5–47.5 g. of crude product, boiling at 110–125°/3 mm. Refractionation gives 41–45 g. (81–88%) of 3-acetamido-2-butanone; b.p. 102–106°/2 mm.; n_D^{25} 1.4558–1.4561 (Note 7).

2. Notes

1. A commercial c.p. grade can be used. The checkers used Merck A.R. grade.
2. A commercial grade, 95% minimum assay, can be used. The checkers used Merck A.R. grade.
3. Any good commercial-grade material appears satisfactory.
4. Reducing the molar ratio of pyridine or anhydride to the amino acid reduces the yield.
5. Without stirring the yield is 46%.
6. With other amino acids, notably glycine and sarcosine, it is necessary to reflux the reactants 1–6 hours.

7. The checkers found it necessary to heat the column to obtain the maximum available product.

3. Methods of Preparation

This method, an adaptation of a previously described procedure,[2,3,4] has been used with a variety of amino acids and anhydrides to give the following products: 1-phenyl-1-propionamido-2-butanone (75%);[5] acetamidoacetylacetone (60%);[5] N-methylacetamidoacetone;[6] 1-phenyl-2-acetamido-3-butanone (79%);[7] 1-phenyl-2-propionamido-3-pentanone (41%);[7] 1-phenyl-2-butyramido-3-hexanone (27%);[7] α-benzamidopropiophenone (42%);[7] α-benzamido-β-phenylpropiophenone (44%);[7] 1-phenyl-1-acetamidoacetone (72–90%);[8,9] 1-phenyl-1-benzamidoacetone (65%);[8] 1-phenyl-2-benzamido-3-butanone (78%);[8] 3-benzamido-2-butanone (65–88%);[8] and 3-acetamido-5-methyl-2-hexanone (73%).[10]

[1] University of Louisville, Louisville, Kentucky.

[2] Dakin and West, *J. Biol. Chem.*, **78**, 91, 757 (1928).

[3] Levene and Steiger, *J. Biol. Chem.*, **74**, 689 (1927); **79**, 95 (1928).

[4] Wiley, *J. Org. Chem.*, **12**, 43 (1947).

[5] Wiley and Borum, *J. Am. Chem. Soc.*, **70**, 2005 (1948).

[6] Wiley and Borum, *J. Am. Chem. Soc.*, **72**, 1626 (1950).

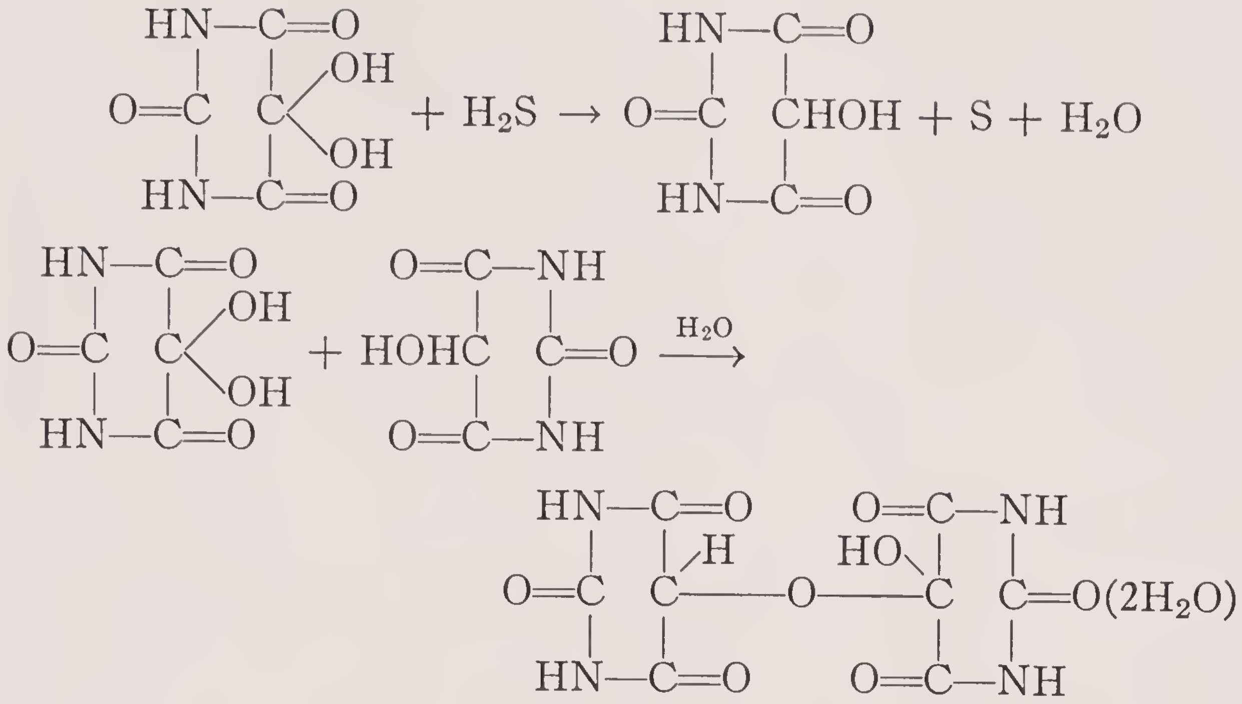
[7] Cleland and Niemann, *J. Am. Chem. Soc.*, **71**, 841 (1949).

[8] Searles and Cvejanovich, *J. Am. Chem. Soc.*, **72**, 3200 (1950).

[9] Rondestvedt, Manning, and Tabibian, *J. Am. Chem. Soc.*, **72**, 3183 (1950).

[10] Borum, Ph.D. Thesis, University of North Carolina, 1949.

ALLOXANTIN DIHYDRATE



Submitted by R. Stuart Tipson.[1]
Checked by T. L. Cairns and F. S. Fawcett.

1. Procedure

An apparatus is assembled in the hood, as shown in Fig. 1. In the 2-l. globe-shaped separatory funnel *H* (stopcock *J* closed) is placed 1.3 l. of deaerated water (Note 1). Three-holed rubber stopper *G* (bearing the stem of a 125-ml. separatory funnel *C* with stopcock *D* closed, a long inlet tube *E*, and a short outlet tube *F*) is inserted in the neck of *H*. In the neck of *C*, a rubber stopper *B*, provided with an inlet tube *A*, is inserted. *H* is flushed with nitrogen (Note 2) admitted at *E*. To the water is added 16.0 g. (0.1 mole) of alloxan monohydrate (Note 3), and the mixture is stirred by the flow of nitrogen through *E* until the alloxan monohydrate has dissolved. The nitrogen flow is discontinued, and hydrogen sulfide (Note 4) is passed in at *E* until the mixture is saturated with this gas and the aqueous solution is free from opalescence (about 2 hours). Carbon disulfide (100 ml.) is now added, and the mixture is agitated for 5 minutes by means of the hydrogen sulfide gas stream. The carbon disulfide layer is then cautiously withdrawn through *J* and discarded, and the aqueous solution is washed once more with 100 ml. of carbon disulfide which is separated and discarded. The hydrogen sulfide flow is discontinued, and nitrogen is passed in at *E* for about 2 hours or until the gas emerging at *F* gives no more than a faint test for hydrogen sulfide with lead acetate paper.

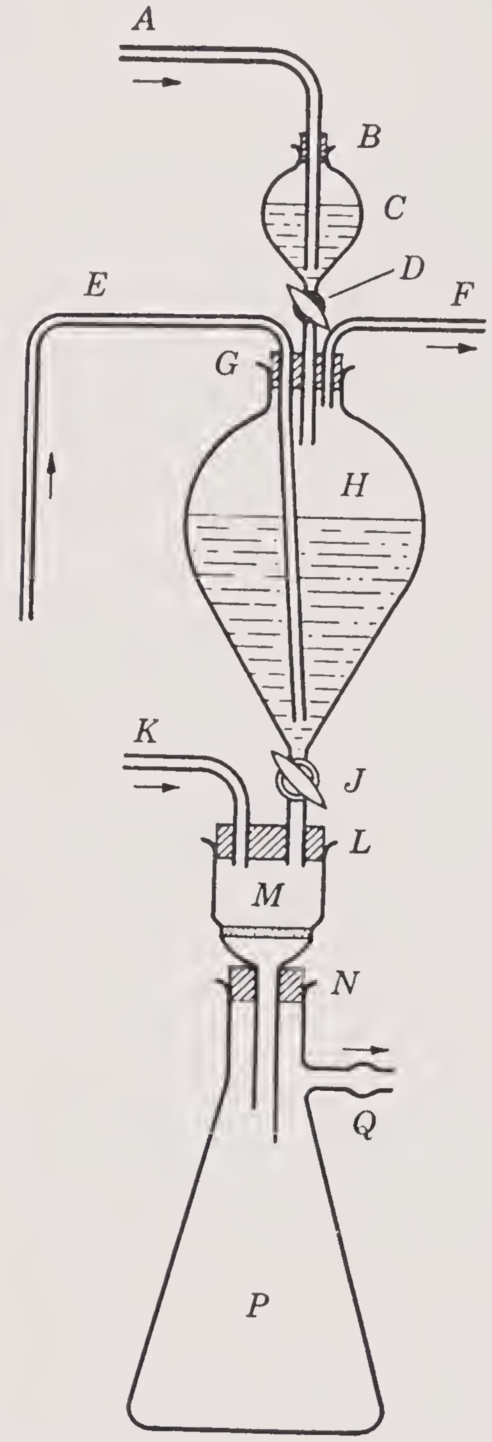


FIG. 1. Apparatus for preparation of alloxantin dihydrate.

Tubes *E* and *F* are now closed, stopper *B* is loosened, and *C* is flushed out with nitrogen admitted through tube *A*. Deaerated water (100 ml.) is placed in *C*, which is then flushed with nitrogen. To this water is added alloxan monohydrate (16.0 g.; 0.1 mole), and the mixture is stirred with *A*, while the nitrogen stream is continued, until the solid has dissolved. *B* is now pushed down to give a tight fit, a slight pressure of nitrogen is applied (at *A*), *F* and *D* are opened, and the solution is allowed to pass from *C* into *H*. To wash out traces of alloxan, a further 10 ml. of water is placed in *C* and run into *H*. *D* is closed, and nitrogen is passed in at *E* and out of *F* until the solutions are thoroughly mixed. *E* and *F* are now closed, and the mixture in *H* is allowed to stand until crystallization is complete (overnight). In the meantime, the stem of funnel *H* is inserted in one hole of the two-holed rubber stopper *L* (also bearing inlet tube *K*); *L* is inserted in the mouth of *M* (a 150-ml., Pyrex Büchner funnel with coarse, fritted-glass septum); and the stem of *M* is inserted in the rubber stopper *N* placed in the neck of a 2-liter Büchner flask *P* (side arm, *Q*). To flush out *M* and *P*, nitrogen is passed in at *K* and out of *Q*. *K* and *Q* are now closed, *F* is opened, and a slight pressure of nitrogen is applied at *F*. *Q* and *J* are opened, and, if necessary, slight suction is applied at *Q*. When all the suspension has passed out of *H*, the nitrogen stream is continued for a few minutes, to remove as much as possible of the liquid clinging to the precipitate in *M*. Then *F*, *J*, and *Q* are closed. The Büchner funnel *M* and its contents are quickly removed, placed in a vacuum desiccator (preflushed with nitrogen), and dried to constant weight, at room temperature, over phosphorus pentoxide and soda-lime. The yield is 27–27.5 g. (84–85%) (Notes 5, 6, and 7).

2. Notes

1. Deaerated water is prepared as follows. A boiling stone is added to distilled water which is then boiled under reflux for at least 5 minutes; it is cooled in ice to room temperature under an atmosphere of oxygen-free nitrogen.

2. For preparation of moist, oxygen-free nitrogen, the commercial gas is passed through (*a*) a 500-ml. Drechsel bottle containing a fresh solution of 25 g. of sodium hydroxide plus 5 g. of pyrogallol in 250 ml. of deaerated water, (*b*) a reversed, empty 500-ml. bottle, and (*c*) a 500-ml. bottle containing 250 ml. of deaerated water.

3. Alloxan monohydrate from Eastman Kodak Company is satisfactory. It is dried to constant weight over soda-lime and phosphorus pentoxide in the vacuum desiccator at room temperature. It should be colorless, and readily and completely soluble in 5 volumes of cold water. The sample employed assayed 99–100% alloxan monohydrate by Tipson and Cretcher's method.[2]

4. Commercial hydrogen sulfide is passed through a (reversed) empty 500-ml. Drechsel gas-washing bottle and then through 250 ml. of deaerated water in a similar bottle (not reversed).

5. The solubility of alloxantin dihydrate in water at room temperature is about 0.29 g. per 100 ml. of solution.[3] An additional 4 g. of product may be obtained by evaporation of the

mother liquor to dryness at 25° under reduced pressure (nitrogen atmosphere).

6. The yield is slightly less if traces of crystals are left adhering to the inner walls of funnel *H*. The alloxantin obtained by dehydration of the product at 120–150° under reduced pressure for 2 hours melts with decomposition in 0.5 to 1 minute when placed in a block heated to 245°.[4]

7. The submitter reports that with minor modification the above hydrogen sulfide reduction procedure can be applied to the preparation of the *dialuric acid monohydrate* intermediate. The apparatus is assembled as in Fig. 1 with the exception that funnel *C* and its accessories are deleted. The above reduction procedure is followed initially, employing 500 ml. of deaerated water and 50 g. of alloxan monohydrate instead of the quantities shown above. After the saturation with hydrogen sulfide (determined by weighing) and the first agitation with carbon disulfide have been conducted as above, the funnel is assembled for filtration in an atmosphere of hydrogen sulfide (rather than nitrogen), and the suspension in *H* is filtered through *M* by manipulations analogous to those described. The colorless crystals of dialuric acid monohydrate are washed on the filter with an additional 100 ml. of carbon disulfide added portionwise via *H*, and, while wet with carbon disulfide and hydrogen sulfide, the crystals and funnel *M* are transferred to a shielded vacuum desiccator and dried over soda-lime and phosphorus pentoxide under high vacuum (Dry Ice-cooled trap). The yield is 44–44.5 g. (87–88%). Even at 300°, the compound exhibits no true melting or gas evolution. Heated at 2° per minute in an aluminum block (initial temperature, 150°) it appears unchanged at 200°, turns faintly pink at 203–206°, and gradually becomes reddish brown (229–232°) and then purplish black at about 270°.

3. Methods of Preparation

Methods of preparation are reviewed in *Org. Syntheses*, **23,** 8 (1943).

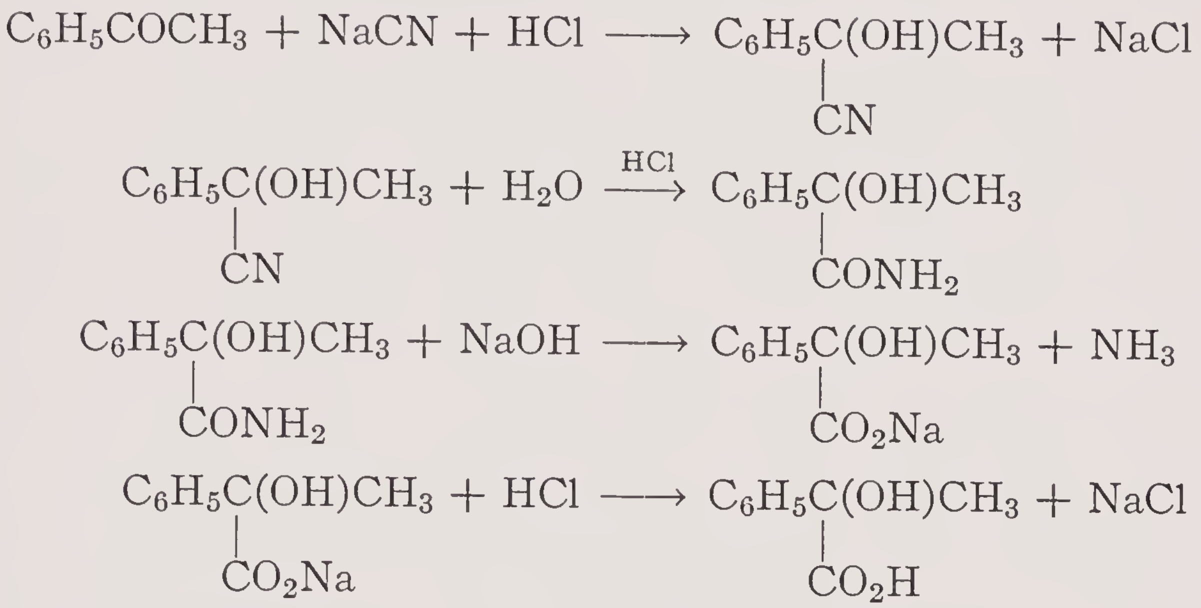
[1] Mellon Institute of Industrial Research, Pittsburgh, Pennsylvania.

[2] Tipson and Cretcher, *Anal. Chem.*, **22**, 822 (1950). See also *Org. Syntheses*, **32**, 6 (1952).

[3] Thunberg, *Skand. Arch. Physiol.*, **33**, 217 (1916) [*C. A.*, **11**, 456 (1917)]; Biilmann and Bentzon, *Ber.*, **51**, 522 (1918).

[4] Nightingale, *Org. Syntheses*, **23**, 6 (1943).

ATROLACTIC ACID



$$C_6H_5COCH_3 + NaCN + HCl \longrightarrow C_6H_5\underset{\underset{CN}{|}}{C}(OH)CH_3 + NaCl$$

$$C_6H_5\underset{\underset{CN}{|}}{C}(OH)CH_3 + H_2O \xrightarrow{HCl} C_6H_5\underset{\underset{CONH_2}{|}}{C}(OH)CH_3$$

$$C_6H_5\underset{\underset{CONH_2}{|}}{C}(OH)CH_3 + NaOH \longrightarrow C_6H_5\underset{\underset{CO_2Na}{|}}{C}(OH)CH_3 + NH_3$$

$$C_6H_5\underset{\underset{CO_2Na}{|}}{C}(OH)CH_3 + HCl \longrightarrow C_6H_5\underset{\underset{CO_2H}{|}}{C}(OH)CH_3 + NaCl$$

Submitted by Ernest L. Eliel and Jeremiah P. Freeman.[1]
Checked by Arthur C. Cope, William F. Gorham, and Roscoe A. Pike.

1. Procedure

Caution! This preparation must be conducted in a hood to avoid exposure to the poisonous hydrogen cyanide that is evolved.

In a 1-l. three-necked round-bottomed flask equipped with a Hershberg stirrer, a thermometer, and a 250-ml. dropping funnel are placed 80 g. (0.666 mole) of acetophenone, 60 ml. of ether, and 100 ml. of water. The apparatus is assembled in a well-ventilated hood, the flask is surrounded by an ice-salt bath, and 82 g. (1.67 moles) of granulated sodium cyanide is added all at once with vigorous stirring. When most of the sodium cyanide has dissolved and the temperature of the mixture has fallen to 5°, 140 ml. (1.7 moles) of concentrated hydrochloric acid is added from the dropping funnel at such a rate that the temperature remains between 5° and 10°. The addition requires about 1.7 hours. After all the acid has been added, the cooling bath is removed and vigorous stirring is continued for 2 hours. The mixture is allowed to settle, and the liquid portion is decanted into a 1-l. separatory funnel. The water layer is returned to the reaction flask, and 100 ml. of water is added to dissolve the salts. The aqueous solution is extracted with four 50-ml. portions of ether, and the original ether layer and extracts are combined in a 500-ml. round-bottomed flask. The ether is distilled at 20–30 mm. pressure (water aspirator) (Note 1), and the residual oil is poured slowly with stirring into 160 ml. of concentrated hydrochloric acid in a 1-l. round-bottomed flask. The mixture then is saturated with hydrogen chloride gas in the hood (Notes 2 and 3) and allowed to stand overnight.

Part of the excess hydrogen chloride is removed by blowing (or drawing) air through the solution for 1 hour. The solution then is made alkaline by the slow addition of 50% aqueous sodium hydroxide (Note 4) with mechanical stirring and cooling in an ice bath. Solid sodium hydroxide (24 g.) is added, and the mixture is steam-distilled until no more ammonia and acetophenone pass into the distillate (Note 5). About 3–4 l. of distillate is collected (Note 6).

Water is added to the residue if necessary to make the volume 700 ml., and the solution is treated with 2 g. of Norit and filtered with suction (Note 7). The filtrate is extracted with 100 ml. of ether (which is discarded), and acidified by the addition of 80 ml. of concentrated hydrochloric acid. After thorough chilling, preferably overnight in a refrigerator, the precipitated atrolactic acid is collected on a suction filter (Note 8) and air-dried at a temperature not exceeding 65°.

The crude product weighs somewhat more than 70 g. and contains water and sodium chloride. It is dissolved in 500 ml. of boiling benzene, the solution is filtered by gravity, and the solid in the flask and funnel is rinsed with 50 ml. of boiling benzene. The filtrate is concentrated by distillation until no more water collects in the distillate, and the residual solution

(300–400 ml.) is cooled. The atrolactic acid which crystallizes is collected on a suction filter and washed with 25 ml. of cold benzene and 25 ml. of commercial pentane (b.p. 30–40°). After air-drying, the cream-colored product amounts to 42.9–43.5 g., m.p. 88–90° with shrinking at 82° (Notes 9 and 10). It is pure enough for most purposes but is intermediate in composition between the anhydrous acid and hemihydrate and contains about 3% sodium chloride. This product is dissolved in 200 ml. of boiling water and treated with 10 g. of Norit. The solution is filtered and cooled overnight at 0–5°. The pure, colorless crystals of atrolactic acid hemihydrate that separate are collected on a suction filter and air-dried. The yield is 33.5–34.7 g. (29–30%), m.p. 88–90° with softening beginning at 75°. The anhydrous acid can be obtained by drying the hemihydrate at 55°/1–2 mm.; m.p. 94.5–95°.

2. Notes

1. By maintaining ebullition with a capillary air inlet and cooling the receiver in a bath containing Dry Ice and trichloroethylene, the distillation can be completed in 1 hour or less.

2. The solution becomes homogeneous when it is nearly saturated. An exothermic reaction begins within a few minutes, and some hydrogen chloride gas escapes.

3. The preparation should be carried to this point in 1 day; the time required is about 8 hours. All the operations must be conducted in a well-ventilated hood.

4. About 150 g. of the 50% sodium hydroxide solution is required.

5. The distillation flask should be heated so as to maintain a liquid volume of 600–700 ml.

6. Acetophenone (15–16.5 g., b.p. 92–94°/20 mm.) can be recovered by extracting the distillate with 100 ml. of pentane (b.p. 30–40°). The extract is dried over sodium sulfate, concentrated, and distilled.

7. Only a small amount of solid, in addition to the Norit, should be retained by the filter. If a copious precipitate of

sodium atrolactate forms, it should be dissolved by the addition of more water.

8. Only small amounts of crude atrolactic acid are recovered by extracting the filtrate with ether.

9. If the yield is low, the mother liquors should be concentrated to a volume of 50 ml. A second crop of crystals can sometimes be obtained in that way.

10. The submitters have obtained the same yields in preparations on five times this scale.

3. Methods of Preparation

Atrolactic acid has been prepared by the oxidation of hydratropic acid with alkaline permanganate,[2] by hydrolysis of α-chloro or α-bromohydratropic acid,[3,4] by sodium amalgam reduction of β,β-dibromoatrolactic acid,[5] from α-aminohydratropic acid and nitrous acid,[6,7] by permanganate oxidation of 2,5-dihydroxy-2,5-diphenyl-3-hexyne,[8] by reaction of ethyl phenylglyoxylate with methylmagnesium iodide followed by hydrolysis,[9] from pyruvic acid and phenylmagnesium bromide,[10] and from α,α-dibromopropiophenone and sodium hydroxide.[11] The last method could not be adapted to the preparation of the acid in large quantities by the submitters.

The synthesis of atrolactic acid through acetophenone cyanohydrin was first described by Spiegel [12] and has since been used by several other investigators.[6,13–17] The above preparation is adapted from the methods of McKenzie and Clough [15] and Freudenberg, Todd, and Seidler.[17]

[1] University of Notre Dame, South Bend, Indiana.

[2] Ladenburg and Rugheimer, *Ber.*, **13**, 375 (1880); Ladenburg, *Ann.*, **217**, 107 (1883).

[3] McKenzie and Clough, *J. Chem. Soc.*, **97**, 1022 (1910).

[4] Merling, *Ann.*, **209**, 21 (1881); Fittig and Wurster, *Ann.*, **195**, 153 (1879); Fittig and Kast, *Ann.*, **206**, 24 (1880).

[5] Bottinger, *Ber.*, **14**, 1238 (1881).

[6] Tiemann and Kohler, *Ber.*, **14**, 1976 (1881).

[7] McKenzie and Clough, *J. Chem. Soc.*, **101**, 397 (1912).

[8] Dupont, *Compt. rend.*, **150**, 1524 (1910); *Ann. chim. Paris*, [8] **30**, 532 (1913).

[9] Grignard, *Compt. rend.*, **135**, 628 (1902); *Ann. chim. Paris*, [7] **27**, 556 (1902).

[10] Peters, Griffith, Briggs, and French, *J. Am. Chem. Soc.*, **47**, 453 (1925).
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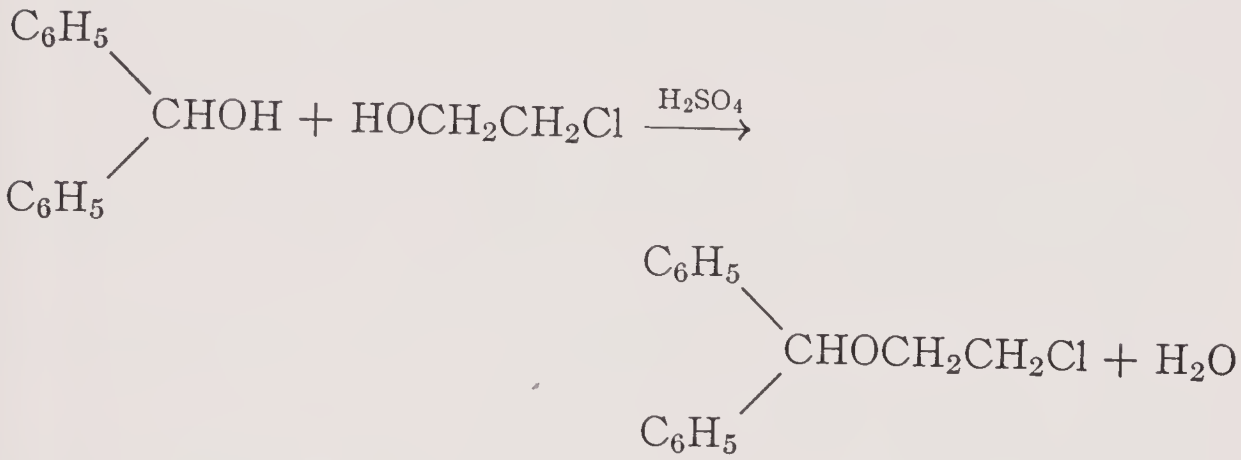
[12] Spiegel, *Ber.*, **14**, 1352 (1881).
[13] Staudinger and Ruzicka, *Ann.*, **380**, 289 (1911).
[14] Smith, *J. prakt. Chem.*, **84**, 731 (1911).
[15] McKenzie and Clough, *J. Chem. Soc.*, **101**, 393 (1912).
[16] McKenzie and Wood, *J. Chem. Soc.*, **115**, 833 (1919).
[17] Freudenberg, Todd, and Seidler, *Ann.*, **501**, 213 (1932).

BENZHYDRYL β-CHLOROETHYL ETHER

(Ether, benzohydryl 2-chloroethyl)



$$\overset{\mathrm{C_6H_5}}{\underset{\mathrm{C_6H_5}}{\mathrm{CHOH}}} + \mathrm{HOCH_2CH_2Cl} \xrightarrow{\mathrm{H_2SO_4}} \overset{\mathrm{C_6H_5}}{\underset{\mathrm{C_6H_5}}{\mathrm{CHOCH_2CH_2Cl}}} + \mathrm{H_2O}$$

Submitted by SHIGEHIKO SUGASAWA and KUNIO FUJIWARA.[1]
Checked by N. J. LEONARD, P. D. THOMAS, and L. A. MILLER.

1. Procedure

In a 500-ml. three-necked round-bottomed flask equipped with a sealed stirrer, a reflux condenser, and a dropping funnel are placed 36 g. (0.45 mole) of ethylene chlorohydrin (Note 1), 5 ml. of concentrated sulfuric acid, and 35 ml. of benzene. The mixture is warmed on a water bath, and to it is added, with efficient stirring, a solution of 55 g. (0.30 mole) of benzhydrol (Note 2) in 65 ml. of benzene (Note 3) during 30–50 minutes. The reaction mixture is heated at the reflux temperature for an additional 4 hours with stirring. To the cooled mixture is added about 35 ml. of benzene, and the combined benzene layer is washed with water and dried over calcium chloride. The drying agent is removed, the benzene is evaporated, and the residue is distilled under reduced pressure. The benzhydryl β-chloroethyl ether is collected at 144–148°/1.0 mm. (174–177°/4 mm.) as a colorless, viscous oil, n_{D}^{30} 1.5651, which should be removed from the receiver to a beaker or Erlenmeyer flask immediately after the distillation. The oil solidifies to a hard white mass, m.p. 27.4–27.8°, when kept in an ice chest (Note 4). The yield is 60.0–65.3 g. (81–88%).

2. Notes

1. Commercial ethylene chlorohydrin is dried over anhydrous sodium sulfate and distilled before use; b.p. 126–127°(743 mm.). Excess is used to avoid the formation of dibenzhydryl ether as a by-product.
2. Eastman Kodak Company benzhydrol, m.p. 67–67.5°, can be used directly.
3. It is necessary to warm the mixture in order to complete the solution of benzhydrol in the benzene.
4. The checkers found this product to be analytically pure without recourse to further purification.

3. Methods of Preparation

This method is based on the process of the submitters.[2]

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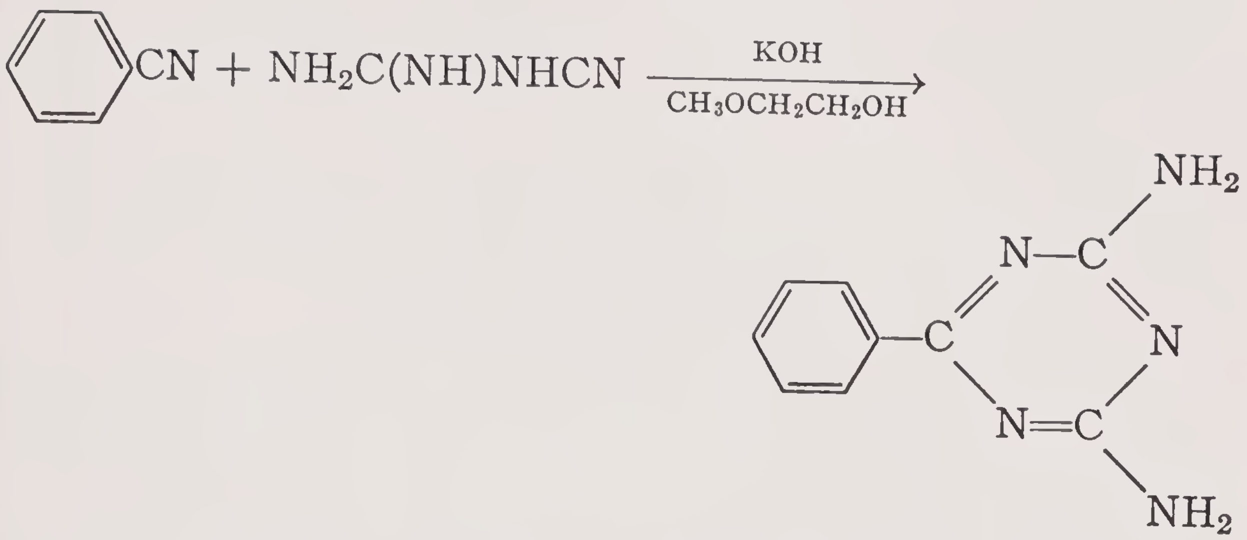
[1] Pharmaceutical Institute, Medical Faculty, University of Tokyo, Tokyo, Japan.

[2] Sugasawa and Fujiwara, *J. Pharm. Soc. Japan*, **71**, 365 (1951) [*C. A.*, **46**, 951*h* (1952)]; Jap. pat. 184,243 (Aug. 12, 1949).

BENZOGUANAMINE

(*s*-Triazine, 2,4-diamino-6-phenyl-)



Submitted by J. K. Simons and M. R. Saxton.[1]
Checked by T. L. Cairns and A. K. Schneider.

1. Procedure

Five grams of potassium hydroxide (85% KOH) is dissolved in 100 ml. of Methyl Cellosolve (Note 1) in a 500-ml. flask (Note 2) fitted with a mechanical stirrer, reflux condenser, and a heating mantle. Dicyandiamide (50.4 g.; 0.6 mole) (Note 3) and benzonitrile (50 g.; 0.485 mole) are added, and the mixture is stirred and heated. A solution is formed, and, when the temperature reaches 90–110°, an exothermic reaction begins and the product separates as a finely divided white solid. The vigor of the reaction is kept under control by the refluxing of the solvent (Note 4).

When the exothermic reaction is ended, the slurry of product is stirred and refluxed for 5 hours to ensure complete reaction (Note 5). The mixture is then cooled and filtered. The product is washed by suspension in hot water (Note 6), filtered, and dried. The yield is 68–79 g. (75–87%). The product melts at 227–228° (Note 7).

1. Notes

1. The commercial solvent is used without purification. Other primary alcohols of similar or higher boiling point are suitable solvents.

2. The large flask is chosen to allow for better stirring and heat transfer.

3. The reaction may be carried out with exactly molar equivalents of reactants. Slightly better yields are obtained by using the 0.2 to 0.25 molar excess of dicyandiamide.

4. Boiling of the Methyl Cellosolve dissipates the heat of reaction, which begins at about 90°. The submitters state that, in one preparation using 100 times the indicated quantities (21-l. flask), two condensers were used and intermittent cooling of the flask with a small stream of water kept the boiling from becoming too violent.

5. Yields reported were obtained after 5 hours under reflux. Preparation of other guanamines indicates an optimum yield after 2.5 hours under reflux.

6. Thorough washing with hot water serves to remove any dicyandiamide or melamine which may be present in the crude product. Benzoguanamine is slightly soluble in hot water.

7. The cellosolve filtrate may be evaporated to obtain further quantities of product, m.p. 227–228°, which raises the total yield to 90–95%.

3. Methods of Preparation

Benzoguanamine has been prepared by the reaction of dicyandiamide with benzonitrile in a sealed tube at 220–230°,[2] with an excess of benzonitrile in the presence of piperidine and potassium carbonate,[3] with benzonitrile in a solvent in the presence of a basic catalyst,[4] and with benzamidine hydrochloride at elevated temperatures.[5] It has also been prepared from the reaction of biguanide acetate with benzamidine hydrochloride,[6] or of biguanide sulfate with benzoyl chloride in an alkaline medium,[7] and by the distillation of guanidine benzoate.[5]

[1] Plaskon Division, Libby-Owens-Ford Glass Company, Toledo 6, Ohio.

[2] Ostrogovich, *Atti accad. Lincei*, [5] **20**, I, 251 [*C. A.*, **5**, 2099 (1911)].

[3] DeBell, Goggin, and Gloor, *German Plastics Practice*, p. 267, DeBell and Richardson, Springfield, Massachusetts, 1946.

[4] Zerweck and Brunner, U. S. pat. 2,302,162.

[5] Ostrogovich, *Atti accad. Lincei*, [5] **20**, I, 185 [*C. A.*, **5**, 2099 (1911)].

[6] Reference 5, p. 252.

[7] Rackmann, *Ann.*, **376**, 181 (1910).

BUTYRCHLORAL

(Butyraldehyde, α,α,β-trichloro-)

$$CH_3CH{=}CHCHO + Cl_2 + H_2O \rightarrow CH_3CHOHCHClCHO + HCl$$

$$CH_3CHOHCHClCHO \rightarrow CH_3CH{=}CClCHO + H_2O$$

$$CH_3CH{=}CClCHO + Cl_2 \rightarrow CH_3CHClCCl_2CHO$$

Submitted by Gus A. Ropp, W. E. Craig, and Vernon Raaen.[1]
Checked by T. L. Cairns and H. N. Cripps.

1. Procedure

Crotonaldehyde (Note 1) (70 g., 1 mole) and 300 ml. of water are stirred with a glass-enclosed bar magnet while chlorine gas is passed in from a cylinder. The reaction vessel, equipped with a water-cooled reflux condenser, is cooled in an ice bath to maintain the temperature at about 10°, and the introduction of chlorine is continued for about 2 hours until the temperature does not rise rapidly when the bath is removed. At this point, the total weight increase is 70–80 g. and the upper oil layer has been converted entirely to a lower layer of viscous white oil. The reaction mixture is heated for 30 minutes at reflux temperature with slow stirring to dehydrate the chlorohydrin. The light-brown oil layer is extracted with chloroform, and the extract (Note 2) is washed twice with water and dried thoroughly over anhydrous magnesium sulfate in the refrigerator. The dry solution is filtered into a thoroughly dried flask (Note 3) equipped with a thermometer, a reflux condenser, and a bubbler tube for the introduction of dry chlorine. Over a period of 2.5 hours, chlorine, passed first through a drying tube filled with Drierite, is introduced. The temperature in the reaction mixture is kept at 0° to 10° by an ice bath, and chlorination is continued until the weight increase indicates that 1 mole of chlorine has been added. The reaction mixture is stirred for 1 hour longer in the ice bath. Then dry carbon dioxide (or nitrogen) is bubbled through the solution at room temperature to remove excess chlorine. The reaction vessel is fitted to a dry 20-mm. by 12-in. Vigreux column wrapped with glass-wool insulation and equipped with a vacuum-jacketed, total take-off-type still head and a water-cooled condenser. The receiver is a dry tared flask with side arm leading to a manometer and, through a Drierite-filled U-tube, to a water pump. Dry carbon dioxide is passed through the still pot during the distillation. The chloroform is distilled (Note 4) at atmospheric pressure. The pressure is then decreased, and the pale yellow butyrchloral is distilled. The yield is 91–93 g. (52–53%); b.p. 57–60°/23 mm.; n_{D}^{25} = 1.4712–1.4740. The oil has a persistent and characteristic but not unpleasant odor (Note 5).

2. Notes

1. Best yields were obtained from Eastman's best-grade crotonaldehyde which had been distilled immediately before use.

2. When this extract is dried and distilled, a high yield of α-chlorocrotonaldehyde, b.p. 147–148°, is obtained. This aldehyde is a powerful lachrymator.

3. Care is necessary to ensure absolute dryness of all glassware in which butyrchloral is contained since the aldehyde quickly forms a solid, insoluble hydrate.

4. If only a moderately pure sample of butyrchloral is needed as a reaction intermediate, the concentrate remaining after evaporation of the chloroform may be used.

5. For best yields, the entire series of reactions should be completed within 1 or 2 days. Distillation at higher pressures tends to cause some decomposition. Analysis of the product showed % Cl, 60.40, 60.64 (calculated % Cl, 60.63).

3. Methods of Preparation

Butyrchloral has been prepared by chlorination of acetaldehyde [2] and of paraldehyde. Butyrchloral hydrate has been prepared by treatment of α,β-dichlorobutyraldehyde with chlorine and water.[3] Butyrchloral has also been prepared [4] by treatment of crotonaldehyde with hydrogen chloride followed by chlorination. Brown and Plump have used a procedure similar to the one described here.[3]

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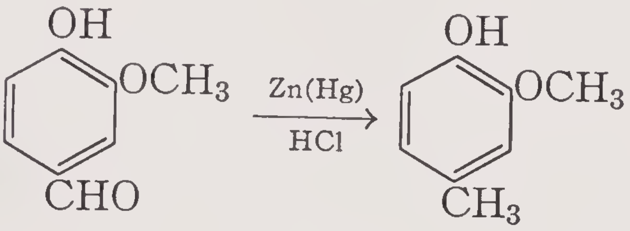
[1] Oak Ridge National Laboratory, Oak Ridge, Tennessee.

[2] Kraemer and Pinner, *Ber.*, **3**, 383 (1870).

[3] Brown and Plump, to Pennsylvania Salt Manufacturing Company, U. S. pat. 2,351,000 (1944) [Brit. pat. 576,435 (1946)].

[4] High, to Udylite Corporation, U. S. pat. 2,280,290 (1942).

CREOSOL



Submitted by R. Schwarz and H. Hering.[1]
Checked by R. L. Shriner and C. L. Furrow, Jr.

1. Procedure

In a 5-l. three-necked flask fitted with a stopper, a reflux condenser, and a 250-ml. dropping funnel are placed 1.5 kg. (22.94 gram atoms) of amalgamated zinc (Note 1) and 800 ml. of concentrated hydrochloric acid. The flask is heated to cause gentle refluxing to occur. A solution of 152 g. (1.0 mole) of vanillin in 450 ml. of 95% ethanol and 1.5 l. of concentrated hydrochloric acid (Note 2) is added dropwise through the dropping funnel over an 8-hour period (Note 3). After the addition of the vanillin is complete the mixture is refluxed for 30 minutes more. The liquid, consisting of two layers, is decanted from the zinc (Note 4) into a 4-l. separatory funnel. The aqueous layer is removed and washed three times with 200-ml. portions of benzene, and the benzene extracts are combined with the crude creosol separated initially. The residual amalgamated zinc is washed twice with 100-ml. portions of benzene, and this benzene solution is added to the combined extracts. The extracts are washed twice with 200-ml. portions of 5% sodium bicarbonate solution, and the resultant precipitate of metallic salts is removed by filtration. The solution is washed once with 200 ml. of water.

The benzene is removed under reduced pressure by distillation on a steam bath. The residue is distilled under reduced pressure, the fraction boiling at 78–79°/4 mm., at 104–105°/15 mm., or at 219–222.5°/760 mm. being collected. A yield of 83–92.5 g. (60–67%) of colorless or pale yellow creosol is obtained, d_4^{25}, 1.092; n_D^{20} 1.5354 (Notes 5 and 6).

2. Notes

1. The amalgamated zinc may be prepared by adding 1500 g. of clean granulated zinc to 600 ml. of 5% mercuric chloride solution. After standing for 2 hours with occasional shaking, the liquid is decanted and the zinc is used immediately.

Alternatively,[2] 1500 g. of granulated zinc is added to a solution of 62.5 g. of mercuric chloride and 62.5 ml. of concentrated hydrochloric acid in 1875 ml. of water. The mixture is shaken for about 5 minutes, the liquid decanted, and the zinc used immediately.

2. The vanillin is first dissolved in ethanol by warming gently, and then 1.5 l. of concentrated hydrochloric acid (d = 1.19) is added. A clear yellow solution is obtained, which soon becomes blue-green.

3. It is advisable to avoid overheating the upper parts of the flask to prevent some brown-red tarry masses from forming.

4. The recovered zinc (900–950 g.) can be used for further preparations by adding more zinc and renewing amalgamation.

5. The submitters report yields up to 103 g. (75%), but this yield could not be consistently obtained by the checkers.

6. The reduction of vanillin by the Clemmensen method using toluene as an auxiliary solvent has been reported.[3] By following these directions, a yield of 49% of creosol was obtained with large amounts of tar.

3. Methods of Preparation

Creosol (also called 2-methoxy-*p*-cresol, 4-methylguaiacol, and 3-methoxy-4-hydroxytoluene) has been obtained by the fractionation of beach creosote tar,[4] by the reduction of vanillin by electrolytic methods,[5,6] by hydrogen and palladium on charcoal or barium sulfate,[7,8] with hydrazine,[9] and by amalgamated zinc and hydrochloric acid.[3,10,11] It has also been prepared by methylation of 4-methylcatechol with methyl iodide [12,13] or with methyl sulfate [14] and is reported to be formed by the distillation of the calcium salt of 3-methoxy-4-hydroxyphenylacetic acid.[15]

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[1] Pharmaceutical-Chemical Institute, Vienna, Austria.

[2] Martin, *Org. Reactions*, **1**, 155 (1942).

[3] Fletcher and Tarbell, *J. Am. Chem. Soc.*, **65**, 1431 (1943).

[4] Mendelsohn, Dissertation, Berlin, 1877, p. 13.

[5] Schepss, *Ber.*, **46**, 2571 (1913).

[6] Shima, *Mem. Coll. Sci. Kyoto*, **A12**, 79 (1929).

[7] Rosenmund and Jordan, *Ber.*, **58**, 162 (1925).

[8] St. Pfau, *Helv. Chim. Acta*, **22**, 550 (1939).

[9] Wolff, *Ann.*, **394**, 100 (1912).

[10] Kawai and Sugiyama, *Ber.*, **72B**, 367 (1939).

[11] Buu-Hoi, Hiong-Ki-Wei, and Royer, *Bull. soc. chim. France*, **12**, 866 (1945).

[12] Ono and Imoto, *J. Chem. Soc. Japan*, **57**, 112 (1936); *Bull. Chem. Soc. Japan*, **11**, 127 (1936).

[13] Steinkopf and Klopfer, *Ber.*, **64B**, 990 (1931).

[14] Fahlberg, Ger. pat. 258,105 [*Frdl.*, **11**, 891 (1912)].

[15] Tiemann and Nagai, *Ber.*, **10**, 206 (1877).

DI-*tert*-BUTYL MALONATE

(Malonic acid, di-*tert*-butyl ester)

$$CH_2(CO_2H)_2 + 2SOCl_2 \rightarrow CH_2(COCl)_2 + 2SO_2 + 2HCl$$

$$CH_2(COCl)_2 + 2t\text{-}C_4H_9OH + 2C_6H_5N(CH_3)_2 \rightarrow CH_2(CO_2t\text{-}C_4H_9)_2 + 2C_6H_5N(CH_3)_2 \cdot HCl$$

Submitted by Chittaranjan Raha.[1]
Checked by William S. Johnson and Rudolph W. Kluiber.

1. Procedure

A. *Malonyl dichloride.* In a 250-ml. Erlenmeyer flask (Note 1) fitted by a ground-glass joint to a reflux condenser capped with a calcium chloride drying tube are placed 52 g. (0.5 mole) of finely powered, dry malonic acid (Note 2) and 120 ml. (about 1.65 mole) of thionyl chloride (Note 3). The flask is warmed for 3 days in a heating bath kept at 45–50° (Note 4). During this period the mixture, which is agitated occasionally by gentle swirling, gradually darkens to a deep brownish red or sometimes a blue color. Finally the mixture is heated at 60° for 5–6 hours. After cooling, it is transferred to a 125-ml. modified Claisen flask and distilled at reduced pressure (water aspirator). A calcium chloride guard tube is inserted between the vacuum line and the apparatus, and the flask is heated with a bath rather than a free flame. After a small fore-run of thionyl chloride, the malonyl chloride distils at 58–60°/28 mm. The pale yellow product amounts to 50.5–60 g. (72–85% yield), n_D^{29} 1.4572.

B. *Di-tert-butyl malonate.* A 1-l. three-necked flask is fitted with a thermometer, a mercury- or rubber sleeve-sealed mechanical stirrer, a reflux condenser protected by a calcium chloride guard tube, and a dropping funnel (either pressure-equalized or protected by a calcium chloride guard tube). A mixture of 100 ml. (about 1 mole) of *tert*-butyl alcohol, dried by distillation from sodium,[2] and 80 ml. (0.63 mole) of dry dimethylaniline (Note 5) is placed in the flask, the stirrer is started, and a solution of 28.0 g. (0.2 mole) of malonyl dichloride in about 60 ml. of dry, alcohol-free chloroform (Note 6) is added slowly from the dropping funnel while the reaction flask is cooled in an ice bath. The reaction is strongly exothermic, and the rate of dropping is regulated so that the temperature of the mixture does not exceed 30°. After the addition is complete (about 30 minutes) the light-greenish mixture is heated under reflux for 4 hours. The mixture is then cooled, 150 ml. of ice-cold 6 *N* sulfuric acid is added with stirring, and the product is extracted with three 250-ml. portions of ether (Note 7). The combined ether extracts are washed once with 6 *N* sulfuric acid, twice with water, twice with 10% potassium carbonate, and once with saturated sodium chloride, and are finally dried over anhydrous sodium sulfate to which a small amount of potassium carbonate is added. The ether is removed by distillation at reduced pressure (water aspirator), and the residue (to which a pinch of magnesium oxide is added) is distilled at reduced pressure from a modified Claisen flask (Note 8). The yield of colorless di-*tert*-butyl malonate, distilling at 65–67°/1 mm., 110–111°/22 mm., is 35.8–36.2 g. (83–84%), n_D^{25} 1.4159, m.p. about −6°.

2. Notes

1. Better results are obtained by using a flat-bottomed flask, which permits the insoluble malonic acid to be distributed over a greater surface.

2. The reaction mixture is heterogeneous at first, and if the acid is not finely powdered, some of it remains unreacted. Attempts to carry out the reaction on a larger scale resulted in some charring and lower yields.

3. Eastman Kodak Company white-label quality thionyl chloride is satisfactory.

4. The temperature range is critical, and yields are lower if it is not controlled carefully. The use of pyridine as a catalyst is not recommended as it produces charring even after relatively short reaction periods.

5. J. T. Baker dimethylaniline (purified grade) is satisfactory without distillation.

6. The chloroform was dried over and distilled from anhydrous calcium chloride just before use.

7. The dimethylaniline may be recovered from the aqueous layer where it is dissolved as the salt.

8. Di-*tert*-butyl malonate, like most *tert*-butyl esters, decomposes readily on heating in the presence of traces of acids. It is therefore desirable to give all glassware to be used for distillation of the material an alkali rinse before use. The addition of a small amount of magnesium oxide also helps to inhibit the decomposition during distillation.[3] When decomposition starts, foaming is generally observed. In this event the addition of glass wool to the distillation flask helps to keep the product from foaming over.

3. Methods of Preparation

Malonyl dichloride has been prepared from malonic acid and thionyl chloride,[4–9] and from carbon suboxide and anhydrous liquid hydrogen chloride.[10] This procedure is based on that of Staudinger and Bereza [6] and of Backer and Homan.[8]

Di-*tert*-butyl malonate has been prepared by the reaction of malonyl dichloride and *tert*-butyl alcohol in the presence of a base,[8, 11] and of malonic acid with isobutylene in the presence of sulfuric acid.[3] The present procedure was based on the former method and developed from studies initiated by P. C. Mukharji of the University College of Science and Technology, Calcutta.

[1] Organic Chemistry Division, Bose Research Institute, Calcutta, India.

[2] *Org. Syntheses*, **30**, 20 (1950), Note 2.

[3] Fonken and Johnson, *J. Am. Chem. Soc.*, **74**, 831 (1952).

[4] Auger, *Ann. chim. et phys.*, [6] **22**, 347 (1891).

[5] Asher, *Ber.*, **30**, 1023 (1897).

[6] Staudinger and Bereza, *Ber.*, **41**, 4463 (1908).

[7] von Auwers and Schmidt, *Ber.*, **46**, 477 (1913).

[8] Backer and Homan, *Rec. trav. chim.*, **58**, 1048 (1939).

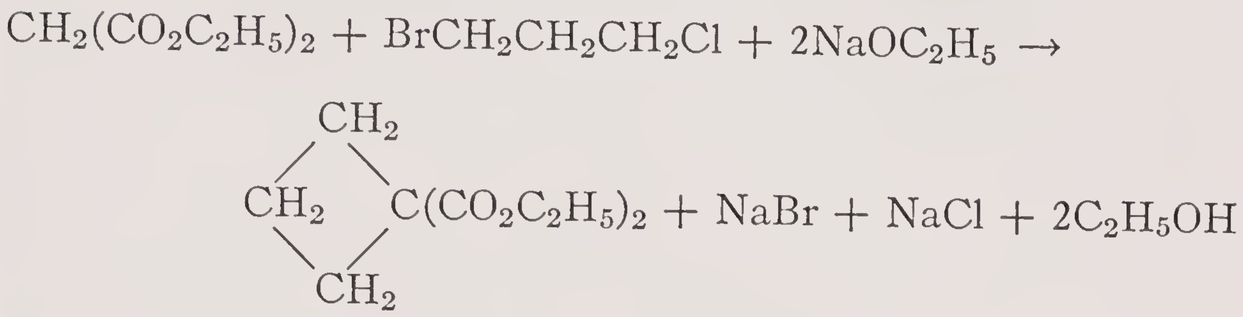
[9] McMaster and Ahmann, *J. Am. Chem. Soc.*, **50**, 145 (1928).

[10] Diels and Wolf, *Ber.*, **39**, 696 (1906).

[11] Backer and Lolkema, *Rec. trav. chim.*, **57**, 1234 (1938).

DIETHYL 1,1-CYCLOBUTANEDICARBOXYLATE

(1,1-Cyclobutanedicarboxylic acid, diethyl ester)



$$CH_2(CO_2C_2H_5)_2 + BrCH_2CH_2CH_2Cl + 2NaOC_2H_5 \rightarrow (CH_2)_3C(CO_2C_2H_5)_2 + NaBr + NaCl + 2C_2H_5OH$$

Submitted by Raymond P. Mariella and Richard Raube.[1]
Checked by William S. Johnson, William DeAcetis, and Herbert Title.

1. Procedure

A solution of sodium ethoxide is prepared by adding 138 g. (6.00 gram atoms) of fresh-cut sodium in small pieces to 2.5 l. of absolute ethanol in a 5-l. round-bottomed flask fitted with an efficient reflux condenser capped with a calcium chloride drying tube (Note 1). In a three-necked 5-l. round-bottomed flask, equipped with a reflux condenser capped with a calcium chloride tube, a rubber-sealed mechanical stirrer, and an inlet tube for addition of the sodium ethoxide solution, are mixed 480 g. (3.00 moles) of diethyl malonate (Note 2) and 472 g. (3.00 moles) of trimethylene chlorobromide (Note 3). The mixture is heated to 80° and vigorously stirred while the sodium ethoxide solution is slowly forced into the flask by means of dry air pressure. The rate of addition is regulated so that the reaction mixture refluxes smoothly. After the addition is complete (this requires about 1.5 hours), the mixture is refluxed, with continued stirring (Note 4), for an additional 45 minutes. Upon completion of the reflux period, the alcohol is removed by distillation (Note 4), 90–95% of the alcohol being recovered. The reaction mixture is cooled, and 900 ml. of cold water is added. After the sodium halides are completely dissolved, the organic layer is separated and the aqueous layer is extracted with three 500-ml. portions of ether. The organic layer and the ether extracts are combined, shaken with 50 ml. of saturated salt solution, and dried over 100 g. of anhydrous sodium sulfate. The solution is filtered, the ether is removed by distillation on a steam bath, and the residue, which weighs 600–625 g., is distilled through a short Vigreux column. The yield of product boiling at 91–96°/4 mm. is 320–330 g. (53–55%)(Note 5).

2. Notes

1. It is important to maintain strictly anhydrous conditions throughout this reaction. The equipment should be carefully predried and the absolute ethanol freshly prepared (preferably by the magnesium ethoxide method [2]) and distilled directly into the reaction flask. If the volume of ethanol is less than 2.5 l. the sodium ethoxide may not remain in solution. It is convenient to employ a three-necked flask carrying two condensers for this operation and to add the sodium through the third neck, which is otherwise kept stoppered.

2. Material boiling at 95.2–95.8°/14 mm., n_D^{25} 1.4120, was used.

3. Trimethylene chlorobromide can be obtained commercially. Material boiling at 141–142°/755 mm., n_D^{25} 1.4843, was used.

4. The stirring must be continued during this operation; otherwise the mixture will bump badly.

5. This material, n_D^{25} 1.433–1.434, d_{20}^{25} 1.042–1.044, is of fair purity and can be hydrolyzed and decarboxylated [3,4] to give cyclobutanecarboxylic acid in more than 80% yield. In order to obtain a highly pure product it may be necessary to fractionally distil the material. For example, on slow redistillation of a product prepared as described above through a 3-ft. Vigreux column at a high reflux ratio, the checkers obtained 8.5% of fore-run n_D^{25} 1.4287–1.4328, 43% of diethyl 1,1-cyclobutanedicarboxylate, n_D^{25} 1.4332–1.4335, and 2.5% of higher-boiling material n_D^{25} 1.4362–1.4427. The pure product is reported to boil at 104.6°/12 mm., 85.2°/3.5 mm., or 60.0°/0.5 mm., n_D^{25} 1.4336, d_{20}^{25} 1.0470.[5]

3. Methods of Preparation

Diethyl 1,1-cyclobutanedicarboxylate has been prepared by the alkylation of diethyl sodiomalonate with trimethylene dibromide [3, 4, 6, 7] or with trimethylene chlorobromide; [5, 8] and by the peroxide-catalyzed addition of hydrogen bromide to diethyl allylmalonate followed by intramolecular alkylation.[9] The procedure described here is that of Mariella and Raube.[5]

[1] Chemical Laboratories of Northwestern University, Evanston, Illinois.

[2] Lund and Bjerrum, *Ber.*, **64**, 210 (1931). See Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 359, D. C. Heath and Company, Boston, Massachusetts, 1941.

[3] *Org. Syntheses*, **23**, 16 (1943).

[4] Cason and Allen, *J. Org. Chem.*, **14**, 1036 (1949).

[5] Mariella and Raube, *Bol. col. quim. Puerto Rico*, 8, 24 (1951) [*C. A.*, **46**, 4491*h* (1952)].

[6] Perkin, *J. Chem. Soc.*, **51**, 1 (1887).

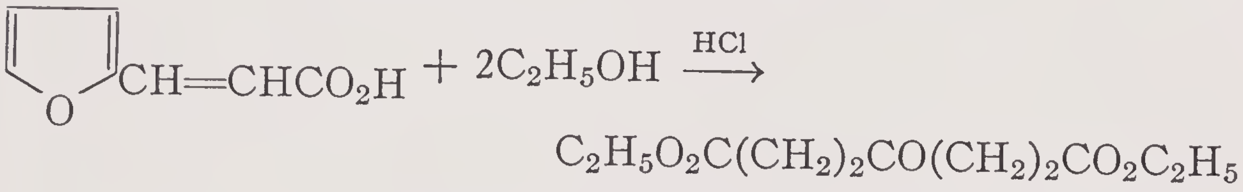
[7] Rupe, *Ann.*, **327**, 183 (1903).

[8] Kishner, *J. Russ. Phys. Chem. Soc.*, **37**, 507 (1905) [*Chem. Centr.*, [2] **76**, 761 (1905).

[9] Walborsky, *J. Am. Chem. Soc.*, **71**, 2941 (1949).

DIETHYL γ-OXOPIMELATE

(Pimelic acid, γ-oxo-, diethyl ester)



$$\text{CH}{=}\text{CHCO}_2\text{H} + 2\text{C}_2\text{H}_5\text{OH} \xrightarrow{\text{HCl}} \text{C}_2\text{H}_5\text{O}_2\text{C(CH}_2)_2\text{CO(CH}_2)_2\text{CO}_2\text{C}_2\text{H}_5$$

Submitted by W. S. Emerson and R. I. Longley, Jr.[1]
Checked by William S. Johnson and I. A. David.

1. Procedure

A 3-l. three-necked flask equipped with a stirrer, reflux condenser, and gas inlet tube is charged with 476 g. (3.45 moles) of furylacrylic acid [2] and 1580 g. (about 33 moles) of 95% ethanol (Note 1). The mixture is heated to boiling, and anhydrous hydrogen chloride is introduced at such a rate that the mixture becomes saturated after 90 minutes. The gas inlet tube is replaced by a stopper, and a 2-ft. Vigreux column is substituted for the reflux condenser. About 250 ml. of solvent is removed by distillation at atmospheric pressure; then another 300 ml. is removed while the pressure is slowly reduced (water aspirator). The residue is cooled and stirred with a solution of about 260 g. of sodium carbonate in water (Note 2). The mixture is extracted with two 250-ml. portions of benzene, and the combined extracts are washed with 100 ml. of water (Note 3). Distillation of the organic portion through a 2-ft. Vigreux column yields, after a small fore-run, 579–657 g. (73–83%) of diethyl γ-oxopimelate, b.p. 116–121°/0.3 mm., n_D^{25} 1.4395–1.4400.

2. Notes

1. If absolute ethanol is used the yield is much lower.
2. A slight excess of sodium carbonate is used. The amount required depends on the amount of hydrogen chloride remaining after the distillation.
3. Sodium chloride may be added if the layers do not separate.

3. Methods of Preparation

Diethyl γ-oxopimelate has been prepared by saturating an ethanol solution of furylacrylic acid [3–7] or γ-oxopimelic acid dilactone [5] with hydrogen chloride. It was found as a by-product in the esterification of furylacrylic acid with ethanol in the presence of *p*-toluenesulfonic acid.[8] This procedure is a modification of the original Marckwald process.[3, 4]

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[1] Monsanto Chemical Company, Dayton, Ohio.

[2] *Org. Syntheses*, **25**, 51 (1945).

[3] Marckwald, *Ber.*, **20**, 2811 (1887).

[4] Marckwald, *Ber.*, **21**, 1398 (1888).

[5] Volhard, *Ann.*, **253**, 206 (1889).

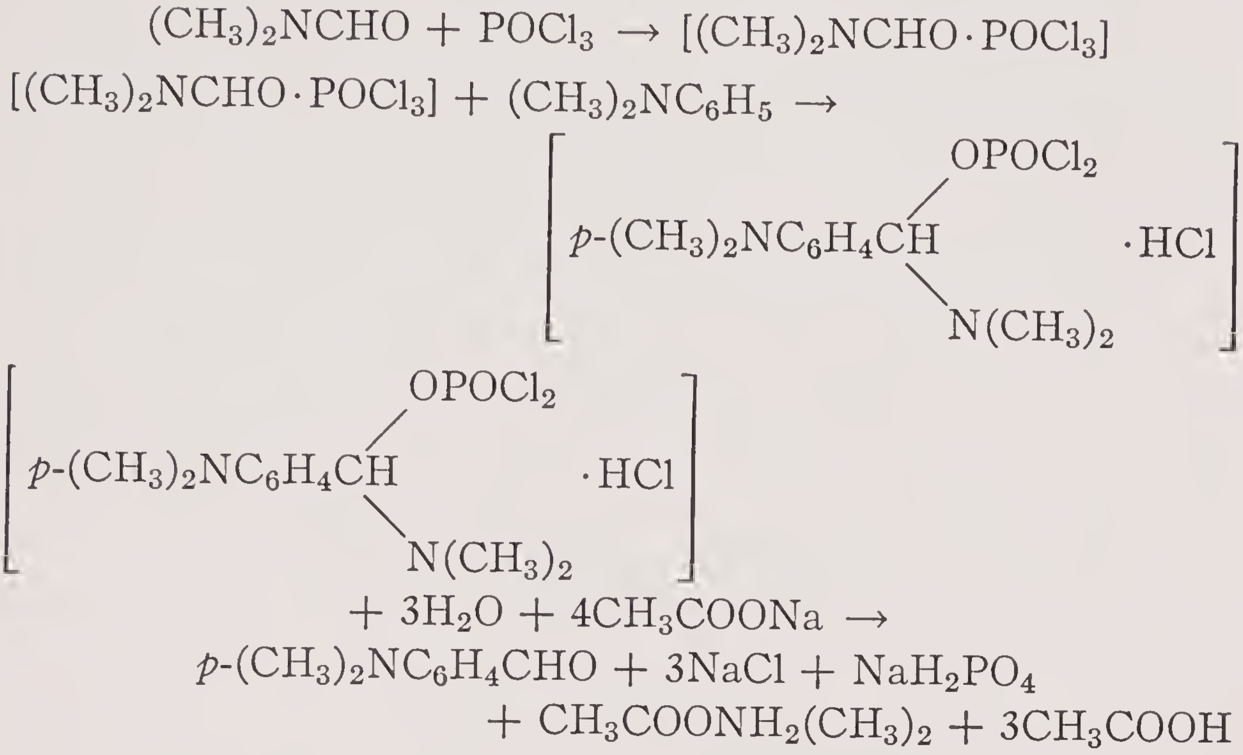
[6] Chichibabin, *Chimie & industrie*, **27**, 563 (1932).

[7] Komppa, *Ann. Acad. Sci. Fennicae*, **A51**, No. 3 (1938) [*C. A.*, **34**, 2335 (1940)].

[8] Murahashi, *Bull. Inst. Phys. Chem. Research* (*Tokyo*), **22**, 476 (1943) [*C. A.*, **42**, 1205 (1948)].

p-DIMETHYLAMINOBENZALDEHYDE

(Benzaldehyde, *p*-dimethylamino-)



$$(CH_3)_2NCHO + POCl_3 \rightarrow [(CH_3)_2NCHO\cdot POCl_3]$$

$$[(CH_3)_2NCHO\cdot POCl_3] + (CH_3)_2NC_6H_5 \rightarrow \left[p\text{-}(CH_3)_2NC_6H_4CH\begin{matrix}\diagup OPOCl_2\\ \diagdown N(CH_3)_2\end{matrix}\cdot HCl\right]$$

$$\left[p\text{-}(CH_3)_2NC_6H_4CH\begin{matrix}\diagup OPOCl_2\\ \diagdown N(CH_3)_2\end{matrix}\cdot HCl\right] + 3H_2O + 4CH_3COONa \rightarrow$$
$$p\text{-}(CH_3)_2NC_6H_4CHO + 3NaCl + NaH_2PO_4 + CH_3COONH_2(CH_3)_2 + 3CH_3COOH$$

Submitted by E. Campaigne and W. L. Archer.[1]
Checked by N. J. Leonard and R. W. Fulmer.

1. Procedure

In a 2-l. three-necked round-bottomed flask, equipped with a sealed stirrer, dropping funnel, and a reflux condenser topped by a calcium chloride tube, is placed 440 g. (6.1 moles) of dimethylformamide (Note 1). While the flask is carefully cooled in an ice bath, 253 g. (1.65 moles) of phosphorus oxychloride is added dropwise with stirring. An exothermic reaction occurs with the formation of the phosphorus oxychloride-dimethylformamide complex. When all the phosphorus oxychloride has been added, and the heat of the reaction has subsided, 200 g. (1.65 moles) of dimethylaniline (Note 2) is added dropwise with stirring. When the addition of the dimethylaniline is complete, a yellow-green precipitate begins to form. The reaction mixture is heated on a steam bath, and stirring is continued for 2 hours. The yellow-green precipitate redissolves when heating is begun. The mixture is then cooled and poured over 1.5 kg. of crushed ice in a 5-l. beaker. Any precipitate that remains in the flask may be washed into the ice mixture with cold water. The solution is neutralized to *p*H 6–8 (Universal Test Paper) by the dropwise addition of approximately 1.5 l. of saturated aqueous sodium acetate with vigorous stirring (Note 3). *p*-Dimethylaminobenzaldehyde begins to precipitate soon after the addition of the sodium acetate is begun. The neutral mixture (total volume about 4.5 l.) is stored in the refrigerator overnight (Note 4). The greenish-tinted crystalline precipitate is filtered by suction, with the aid of a rubber dam, and washed several times with water on the filter. The green color is readily removed during the washing. The very light-yellow to nearly colorless product, after air-drying, weighs 198–208 g. (80–84%) and melts at 73–74°. It is essentially pure and useful for most purposes as obtained (Note 5).

2. Notes

1. The dimethylformamide is available as technical grade DMF from the Grasselli Chemicals Department of E. I. du Pont de Nemours and Company. Dimethylformamide can be prepared by the method of Mitchell and Reid [2] from dimethylamine and formic acid.

2. Dimethylaniline free from monomethylaniline (Eastman Kodak Company) is used.

3. It is possible to neutralize the acid solution partially with sodium hydroxide before the sodium acetate is added, but it is more difficult to avoid localized heating by this method. It is important to keep the reaction mixture below 20° during the neutralization, by the addition of ice if necessary, since any excessive increase in temperature of the aqueous solution leads to the formation of greenish blue dyestuffs, which are very difficult to remove from the product.

4. The mixture may turn orange-colored when allowed to stand overnight.

5. If a purer product is desired, the aldehyde may be purified by the method described by Adams and Coleman.[3]

3. Methods of Preparation

p-Dimethylaminobenzaldehyde has been prepared previously from dimethylaniline, formaldehyde, and *p*-nitrosodimethylaniline in 56–59% yield,[3] by the formylation of dimethylaniline with *N*-methylformanilide in approximately 50% yield,[4] and by the formylation of dimethylaniline with dimethylformamide.[5]

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[1] Indiana University, Bloomington, Indiana.

[2] Mitchell and Reid, *J. Am. Chem. Soc.*, **53**, 1879 (1931).

[3] *Org. Syntheses* Coll. Vol. **1**, 214 (1941).

[4] Vilsmeier and Haack, *Ber.*, **60**, 119 (1927).

[5] Brit. pat. 607,920 [*C. A.*, **43**, 2232 (1949)].

DIMETHYLKETENE

(Ketene, dimethyl-)

$$(CH_3)_2CHCOOH + Br_2 \xrightarrow{P} (CH_3)_2CBrCOBr \xrightarrow{Zn} (CH_3)_2C{=}C{=}O$$

Submitted by C. W. Smith and D. G. Norton.[1]
Checked by T. L. Cairns and J. C. Sauer.

1. Procedure

A. *Preparation of α-bromoisobutyryl bromide.* To a mixture of 250 g. (2.85 moles) of isobutyric acid and 35 g. (1.13 moles) of red phosphorus in a 1-l. three-necked flask, fitted by ground-glass joints to a dropping funnel, mechanical stirrer, and reflux condenser, is added, dropwise with stirring, 880 g. (5.5 moles) of bromine. After the addition is complete, the solution is warmed to 100° over a period of 6 hours. The unreacted bromine and hydrogen bromide are removed under reduced pressure (30 mm.). The α-bromoisobutyryl bromide is decanted from the phosphorous acid and fractionated through a short helices-packed column. After a considerable fore-cut, the main fraction, 493–540 g. (75–83%), is collected at 91–98° (100 mm.).

B. *Preparation of dimethylketene* (Note 1). The apparatus for this preparation consists of a 500-ml. flask equipped with an inlet tube for nitrogen and a dropping funnel and fitted to a 6-in. modified Claisen still head leading to a tared spiral inlet trap having stopcocks on the inlet and exit sides and cooled in Dry Ice-acetone (Note 2). This trap is connected to a vacuum line, and the reaction is carried out at 300 mm. pressure. After 40 g. (0.61 gram atom) of zinc turnings and 300 ml. of ethyl acetate have been placed in the flask and the system has been flushed with nitrogen (free of oxygen and moisture) and heated to incipient boiling, 111 g. (0.483 mole) of α-bromoisobutyryl bromide is added dropwise at such a rate that the ethyl acetate boils gently. A slow stream of nitrogen is continued throughout the reaction. Dimethylketene distils along with ethyl acetate and is obtained in 46–54% yield as a 9–10% solution in ethyl acetate (15–18 g. of dimethylketene in 190–200 ml. of ethyl acetate) (Note 3).

2. Notes

1. This ketene reacts rapidly with oxygen to form an explosive peroxide. Drops of solution allowed to evaporate in air may detonate. Washing with water is an efficient means of decontamination.
2. If simple traps are used, it is necessary to use two in series to condense all the dimethylketene and ethyl acetate.
3. The concentration of dimethylketene is determined by titration of an aliquot at ice temperatures with 0.1 *N* sodium hydroxide using phenolphthalein indicator. Under these conditions, blank determinations indicate that ethyl acetate is not hydrolyzed.

The identity of the dimethylketene may be determined (and an approximate check made on the concentration) by adding 35 g. of dimethylketene solution to 15 g. of aniline in 75 ml. of ether. After 2–3 minutes, the ether solution is washed with dilute hydrochloric acid, dilute potassium carbonate, then water, and the ether is evaporated. Isobutyroanilide, m.p. 102–103° (103–104° after one recrystallization, no melting-point depression in mixture with an authentic sample), is obtained in about 90% yield based on the concentration of dimethylketene indicated by titration.

3. Methods of Preparation

The preparation of ketenes has been discussed by Hanford and Sauer in *Organic Reactions*.[2] Dimethylketene has been prepared by the treatment of α-bromoisobutyryl bromide with zinc,[3] and by the pyrolysis of isobutyrylphthalimide,[4] dimethylmalonic anhydride,[5] or α-carbomethoxy-α,β-dimethyl-β-butyrolactone.[6] Dimethylketene dimer has been prepared by heating isobutyryl chloride with a tertiary amine. Pyrolysis of the dimer yields dimethylketene.[7]

α-Bromoisobutyryl bromide has been prepared in a two-step process involving the bromination of isobutyric acid to α-bromoisobutyric acid followed by treatment with phosphorus tribromide.[8] A one-step process utilizing the Hell-Volhard-Zelinsky reaction [9] is more satisfactory.

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[1] Shell Development Company, Emeryville, California.

[2] Hanford and Sauer, in Adams, *Organic Reactions*, Vol. 3, p. 108, John Wiley & Sons, 1946.

[3] Staudinger and Klever, *Ber.*, **39**, 968 (1906).

[4] Hurd and Dull, *J. Am. Chem. Soc.*, **54**, 2432 (1932).

[5] Staudinger, *Helv. Chim. Acta*, 8, 306 (1925).

[6] Ott, *Ann.*, **401**, 159 (1913).

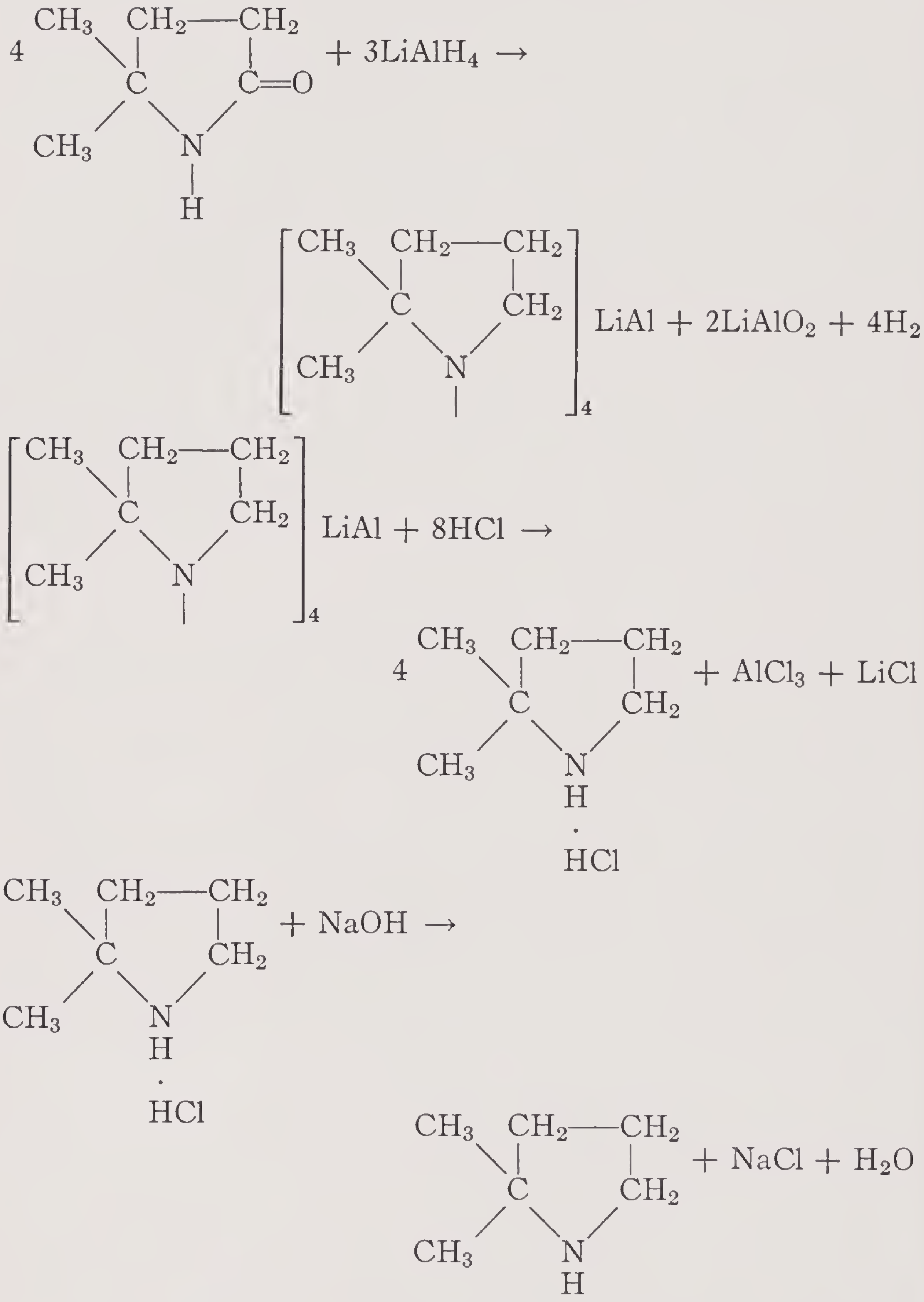
[7] See reference 2, p. 136.

[8] Taufen and Murray, *J. Am. Chem. Soc.*, **67**, 754 (1945).

[9] Volhard, *Ann.*, **242**, 161 (1887).

2,2-DIMETHYLPYRROLIDINE

(Pyrrolidine, 2,2-dimethyl-)



Submitted by Robert Bruce Moffett.[1]
Checked by N. J. Leonard and J. W. Curry.

1. Procedure

A 3-l. three-necked round-bottomed flask is placed on a steam bath and fitted with a mercury-sealed Hershberg stirrer, a dropping funnel, and an efficient reflux condenser topped with a tube containing soda lime and calcium chloride. In this flask are placed 38 g. (1 mole) of pulverized lithium aluminum hydride (Note 1) and 400 ml. of dry tetrahydrofuran (Note 2). The mixture is heated under reflux with stirring for 15 minutes or until most of the lithium aluminum hydride has dissolved. A solution of 90.5 g. (0.8 mole) of 5,5-dimethyl-2-pyrrolidone[2] in 200 ml. of dry tetrahydrofuran (Note 2) is added slowly at such a rate that the solvent refluxes gently without external heating. When the addition is complete and the initial reaction subsides, the mixture is stirred and heated at gentle reflux for 8 hours.

The condenser is then set for downward distillation, and, while the mixture is stirred, about 450 ml. of solvent is distilled (Notes 3 and 4). The condenser is reset in the reflux position, and 300 ml. of ether (commercial anhydrous) is added slowly from the dropping funnel with vigorous stirring. This is followed by 50 ml. of ethyl acetate added very slowly with vigorous stirring and finally by 500 ml. of 6 *N* hydrochloric acid added in the same manner.

The condenser is again set downward, and the dropping funnel is replaced by a tube reaching nearly to the bottom of the flask. Steam is passed in, and the distillation is continued for several minutes after the boiling point reaches 100° (Note 5). The distillate is discarded. The mixture in the flask is cooled, and to it is added carefully 350 ml. of 12 *N* sodium hydroxide with stirring (Note 6). The alkaline mixture is then steam-distilled until the distillate is no longer basic (Note 7).

The 2,2-dimethylpyrrolidine may be recovered from the aqueous distillate in two ways: (*a*) the distillate can be extracted continuously with ether;[3] or (*b*) the distillate can be acidified with hydrochloric acid and concentrated to dryness under reduced pressure to give crude 2,2-dimethylpyrrolidine hydrochloride. The base is then liberated by adding an excess of saturated aqueous sodium hydroxide solution. The oily layer is separated. The aqueous layer and salt are extracted several times with ether, which is combined with the amine. In either case the ether solution is dried thoroughly over anhydrous potassium carbonate (Note 8).

The drying agent is removed by filtration, and the ether is stripped through a short helices-packed column. The residue is fractionally distilled at 103–105°/745 mm.; n_{D}^{20} 1.4330; n_{D}^{25} 1.4304; d_4^{25} 0.8211. The yield is 53–62 g. (67–79%).

2. Notes

1. The hydride can be pulverized rapidly and safely by breaking the large pieces with a spatula, followed by careful crushing with a mortar and pestle. Caution must be observed because the solid may inflame on prolonged grinding or abrasion. The hydride dust is caustic and irritating.

2. Tetrahydrofuran from E. I. du Pont de Nemours and Company can be dried conveniently by adding to it lithium aluminum hydride in small portions until no further reaction (evolution of hydrogen) ensues. After the mixture has been stirred for a few minutes, most of the tetrahydrofuran is distilled from it with stirring (to prevent bumping) (Note 3), and collected in a receiver protected from moisture by a calcium chloride tube.

3. Care must be taken in distilling solutions of lithium aluminum hydride. Explosions have been reported[4] toward the end of distillations of such solutions, especially if they contained carbon dioxide. It is therefore recommended that these distillations be carried out behind a shield and that not more than *three-fourths* of the solvent be removed.

4. If this tetrahydrofuran is collected in a receiver protected from moisture it may be used in subsequent runs.

5. This steam distillation removes ether, tetrahydrofuran, and other volatile neutral products. If too much water accumulates in the flask, it may be heated in an electric heating mantle after most of the ether has been removed.

6. At this point the mixture should be a very strongly basic, mobile, milky slurry.

7. From time to time an aliquot of the distillate being collected can be titrated with standard acid to determine whether significant amounts of amine are distilling.

8. Sufficient drying agent should be used so that no aqueous liquid phase appears.

3. Methods of Preparation

2,2-Dimethylpyrrolidine has been prepared by the hydrogenation of 5-amino-2,2-dimethylpyrroline-N-oxide or 5-imino-2,2-dimethylpyrrolidine in the presence of Raney nickel [5] or by reduction with sodium and alcohol.[5] This method is from unpublished work of the submitter.

[1] The Upjohn Company, Kalamazoo, Michigan.

[2] *Org. Syntheses*, **32**, 59 (1952).

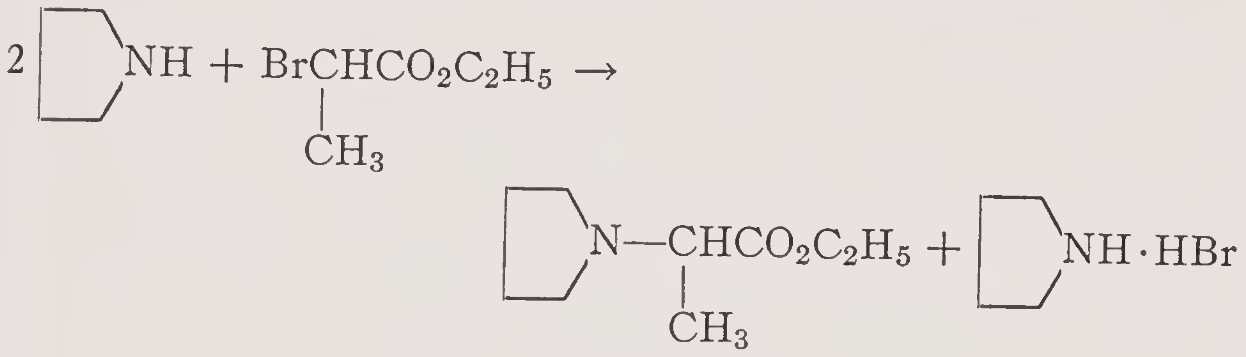
[3] *Org. Syntheses* Coll. Vol. **1**, 277 (1941).

[4] Barbaras, Barbaras, Finholt, and Schlesinger, *J. Am. Chem. Soc.*, **70**, 877 (1948).

[5] Buckley and Elliott, *J. Chem. Soc.*, **1947**, 1508.

ETHYL α-(1-PYRROLIDYL)-PROPIONATE

(1-Pyrrolidineacetic acid, α-methyl-, ethyl ester)



Submitted by Robert Bruce Moffett.[1]
Checked by N. J. Leonard and S. Gelfand.

1. Procedure

A 1-l. three-necked round-bottomed flask is placed on a steam bath and fitted with a stirrer, reflux condenser, and dropping funnel. A solution of 181 g. (1 mole) of ethyl α-bromopropionate in 200 ml. of benzene is placed in the flask (Note 1), and 148 g. (2.1 moles) of pyrrolidine (Note 2) is added slowly with stirring at such a rate that the solvent refluxes gently. When the addition is complete (about 1 hour is required), the mixture is heated under reflux for 1 hour. After being cooled, the mixture is poured into about 500 ml. of ice water and acidified with dilute hydrochloric acid. The aqueous layer is separated, washed once with ether, and made strongly basic with cold 40% sodium hydroxide solution. The basic ester is extracted with four 200-ml. portions of ether. The ether extracts are combined, washed with 100 ml. of water, and dried over anhydrous potassium carbonate. The drying agent is removed by filtration and the ether by distillation. The residue is distilled under reduced pressure through a short fractionating column; b.p. 84°/12 mm. (95–96°/19 mm., 99.5–100.5°/23 mm., 104–105°/30 mm.); n_D^{20} 1.4478, n_D^{25} 1.4450; d_4^{25} 0.9724. The yield is 137–156 g. (80–91%).

2. Notes

1. The yield of product is lowered appreciably if the solution is preheated before addition of the pyrrolidine.

2. Pyrrolidine is obtainable from E. I. du Pont de Nemours and Company, Electrochemicals Division, Niagara Falls, New York.

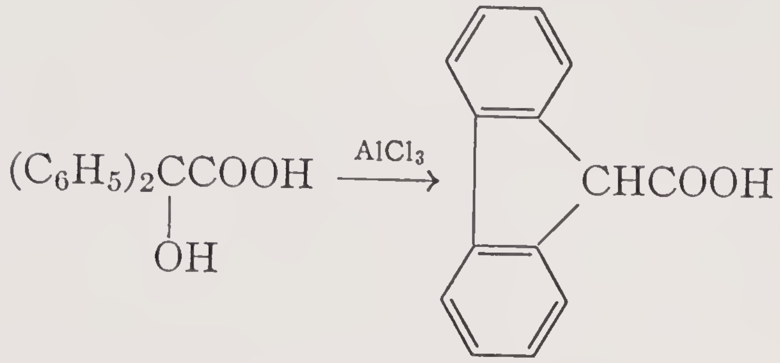
3. Methods of Preparation

Ethyl α-(1-pyrrolidyl)-propionate has been prepared by the reaction of pyrrolidine with ethyl α-bromopropionate.[2]

[1] The Upjohn Company, Kalamazoo, Michigan.

[2] Moffett, *J. Org. Chem.*, **14**, 862 (1949).

9-FLUORENECARBOXYLIC ACID



Submitted by Henry J. Richter.[1]
Checked by Richard T. Arnold, B. C. W. Hummel, and W. J. Wolf.

1. Procedure

Caution! Because of the evolution of considerable amounts of hydrogen chloride, this preparation must be conducted in a good hood or the apparatus must be attached to a gas trap.

A mixture of 45.6 g. (0.2 mole) of benzilic acid (Note 1) in 700 ml. of anhydrous thiophene-free benzene, contained in a 2-l. three-necked flask fitted with a reflux condenser (attached to a calcium chloride drying tube) and a motor-driven sealed stirrer, is cooled in an ice bath until a crystalline mass results. To the stirred mixture is added, in one portion, 80 g. (0.6 mole) of anhydrous aluminum chloride. The stirred mixture is heated until refluxing begins and is maintained at this temperature for 3 hours. During this period much hydrogen chloride is evolved, and the initially yellow solution soon becomes deep red. The solution is cooled and decomposed by the cautious addition of small pieces of ice, and then 400 ml. of water is added cautiously, followed by 200 ml. of concentrated hydrochloric acid. The benzene is removed by steam distillation, and the product is separated by filtration from the hot mixture. The lumps of product are crushed and extracted with 400 ml. of boiling 10% sodium carbonate solution. The mixture is filtered, and the extraction is repeated on the undissolved residue with an additional 200 ml. of hot 10% sodium carbonate solution. The basic filtrates are combined, 3–4 g. of Norit is added, and the mixture is heated to boiling. The Norit is separated by filtration, and the cooled solution is strongly acidified with cold concentrated hydrochloric acid (Note 2). The solid is collected on a Büchner funnel, washed with two 100-ml. portions of water, and dried (Note 3). The 9-fluorenecarboxylic acid so obtained weighs 39–41 g. (93–97%) and melts at 215–222°.

This product can be further purified by stirring it for several minutes with 200 ml. of benzene at 45°. The insoluble portion is collected on a Büchner funnel and washed first with 40 ml. of cold benzene and then with 40 ml. of petroleum ether (b.p. 28–38°). There is thus obtained 30–34 g. (71–81%) of almost colorless 9-fluorenecarboxylic acid melting at 219–222° with some previous sintering (Note 4).

2. Notes

1. The Distillation Products Industries grade melting at 150–151° is satisfactory.

2. Good results are usually obtained if the temperature during neutralization is not allowed to exceed 15°.

3. If the occluded hydrochloric acid and aluminum salts are effectively removed during the washing operation, this product can be dried in a steam oven without discoloration.

4. The melting points reported for this compound range from 210° to 230° [2–6] and appear to be a function of the rate of heating. The product obtained above, showing a neutralization equivalent of 215–218 (calculated 210), has proved very satisfactory. The acid may be further purified by crystallization from 50% ethanol using 5–6 ml./g. There is then obtained 60–70% of acid melting at 221–223° with some previous sintering. All melting points are uncorrected.

3. Methods of Preparation

The procedure described is essentially that of Arnold, Parham, and Dobson [2] based on the reaction reported by Vorlander and Pritzsche.[3] This acid has also been prepared from ethyl tri-chloroacetate in benzene with aluminum chloride,[4] from fluorene by metalation with *n*-butyllithium [5] or sodium triphenylmethyl [6] followed by carbonation, from diphenyleneketene and water,[7] and from 9-fluorenylmagnesium bromide and carbon dioxide.[8]

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[1] Hamline University, St. Paul, Minnesota.

[2] Arnold, Parham, and Dodson, *J. Am. Chem. Soc.*, **71**, 2439 (1949).

[3] Vorlander and Pritzsche, *Ber.*, **46**, 1793 (1913).

[4] Delacre, *Bull. soc. chim. France*, [3] **27**, 875 (1902).

[5] Burtner and Cusic, *J. Am. Chem. Soc.*, **65**, 262 (1943).

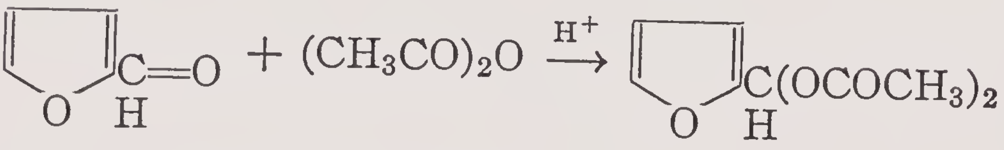
[6] Schlenk and Bergmann, *Ann.*, **463**, 98 (1928).

[7] Staudinger, *Ber.*, **39**, 3064 (1906).

[8] Grignard and Courtot, *Compt. rend.*, **152**, 1493 (1911).

FURFURAL DIACETATE

(2-Furanmethanediol, diacetate)



Submitted by R. T. Bertz.[1]
Checked by James Cason, William G. Dauben, W. B. Fearing, and B. P. Summerer.

1. Procedure

In a 300-ml. Claisen flask, whose side neck is elongated by a 10-cm. indented section, 102 g. (1 mole) of acetic anhydride and 0.1 ml. (Note 1) of concentrated sulfuric acid are mixed by hand swirling. The mixture is cooled to 10° by swirling in an ice bath, then there is added, during about 10 minutes, 96 g. (1 mole) of recently distilled furfural (Note 2). The temperature is maintained at 10–20°. After addition is complete and the contents of the flask have been well mixed by swirling, the cooling bath is removed and the reaction allowed to warm up spontaneously. A maximum temperature of about 35° is usually reached in about 5 minutes. After the temperature has dropped to that of the room (20–30 minutes), 0.4 g. (Note 1) of anhydrous sodium acetate is added, the flask is fitted for distillation at reduced pressure, and the mixture is distilled from an oil bath. A fore-run, weighing 50–70 g. and consisting principally of a mixture of acetic anhydride, furfural, and furfural diacetate (Note 3), is collected at 50–140°/20 mm. (Note 4). The product, collected at 140–142°/20 mm., weighs 129–139 g. (65–70%) and melts at 52–53° (Notes 4 and 5).

2. Notes

1. In order to freeze the equilibrium during distillation, it is imperative that the sulfuric acid catalyst be previously neutralized by sodium acetate; hence it is important that the small quantities of sulfuric acid and sodium acetate be measured carefully.

2. The furfural used by the checkers was collected at 158–163°. In several runs made with technical furfural, which had been stored several years and was black and opaque, a satisfactory product was obtained but yields were 45–53%.

3. This fore-run turns black on standing, but if stored no more than a few days it may be assumed to be an equimolar mixture of furfural and acetic anhydride and may be used as starting material for subsequent runs. If no additional runs are to be made, the yield may be increased by 5–10% by redistilling the fore-run.

4. If collection of the product is started too soon it rapidly darkens and becomes partly liquid on standing. It is advisable to begin collecting the product only after a small sample of distillate, collected separately, sets to a crystalline mass on cooling. Products collected in this manner darkened slightly but remained solid after storage for 2 months. Original distillation of the reaction mixture through a 50-cm. column appeared not to improve the stability to storage, but a sample redistilled in a Claisen flask remained nearly white after storage for 6 months. All stored samples have a strong odor of acetic acid.

5. The submitter has carried out the preparation similarly on a 10-mole scale.

3. Methods of Preparation

Furfural diacetate has been prepared from furfural and acetic anhydride in the presence of various catalysts.[2-4] The present method is adapted to recovery and re-use of unreacted starting materials.

---

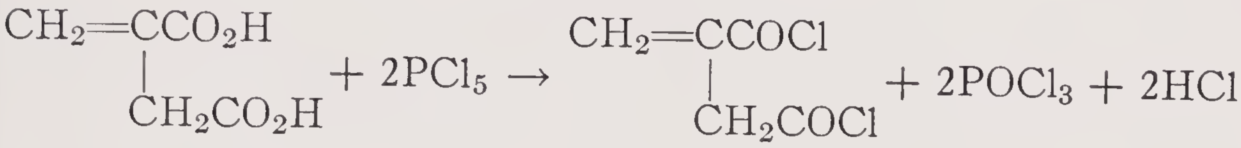
[1] Jacob V. Heemskerklaan 16, Katwyk aan Zee, Holland.

[2] Knoevenagel, *Ann.*, **402**, 119 (1913).

[3] Scheibler, Sotscheck, and Friese, *Ber.*, **57**, 1445 (1924).

[4] Gilman and Wright, *Rec. trav. chim.*, **50**, 833 (1931).

ITACONYL CHLORIDE



$$\begin{array}{l} CH_2{=}CCO_2H \\ \quad| \\ \quad CH_2CO_2H \end{array} + 2PCl_5 \rightarrow \begin{array}{l} CH_2{=}CCOCl \\ \quad| \\ \quad CH_2COCl \end{array} + 2POCl_3 + 2HCl$$

Submitted by Henry Feuer and Stanley M. Pier.[1]
Checked by William S. Johnson and Ernest F. Silversmith.

1. Procedure

In a 500-ml. round-bottomed flask fitted with a reflux condenser and a drying tube leading to a gas-absorption trap [2] are placed 234 g. (1.1 mole) of phosphorus pentachloride (Note 1) and 65 g. (0.5 mole) of itaconic acid (Note 2). The reagents are mixed by shaking the flask; after a few minutes a vigorous reaction commences, resulting in partial liquefaction of the mixture and copious evolution of hydrogen chloride. When the initial reaction subsides, the mixture is gently heated to cause reflux of phosphorus oxychloride until all the solid dissolves; then heating is continued for an additional 15 minutes (Note 3). The reflux condenser is replaced by a 12-in. Vigreux column, and the phosphorus oxychloride is removed by distillation at reduced pressure provided by a water aspirator (Note 4), the major portion coming over at about 45°/85 mm. When all the phosphorus oxychloride has been removed, the pressure is reduced (vacuum pump) and the material boiling at 70–75°/2 mm. is collected. Liquid boiling in this range weighs 50–55 g., representing a yield of 60–65%. This material, n_D^{20} 1.4915, n_D^{25} 1.4900, is pure enough for most purposes, but it may be further refined by distillation through a packed column, yielding 47–53 g. of a water-white liquid, n_D^{20} 1.4919, boiling at 71–72°/2 mm.

2. Notes

1. The slight molar excess of phosphorus pentachloride has been found to increase the yield of product. It is best to use apparatus with ground-glass joints.

2. Chas. Pfizer and Company technical grade itaconic acid was employed without purification.[3]

3. Heating for a longer period results in a rather sudden change in color from pale yellow to deep orange or red, and a decrease in yield.

4. Considerable dissolved hydrogen chloride is liberated at this point and passes into the water aspirator. A mechanical vacuum pump should not be used at this stage because it would be damaged by corrosion.

3. Methods of Preparation

Itaconyl chloride has been prepared previously only by the reaction of itaconic anhydride with phosphorus pentachloride.[4]

[1] Purdue University, Lafayette, Indiana.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

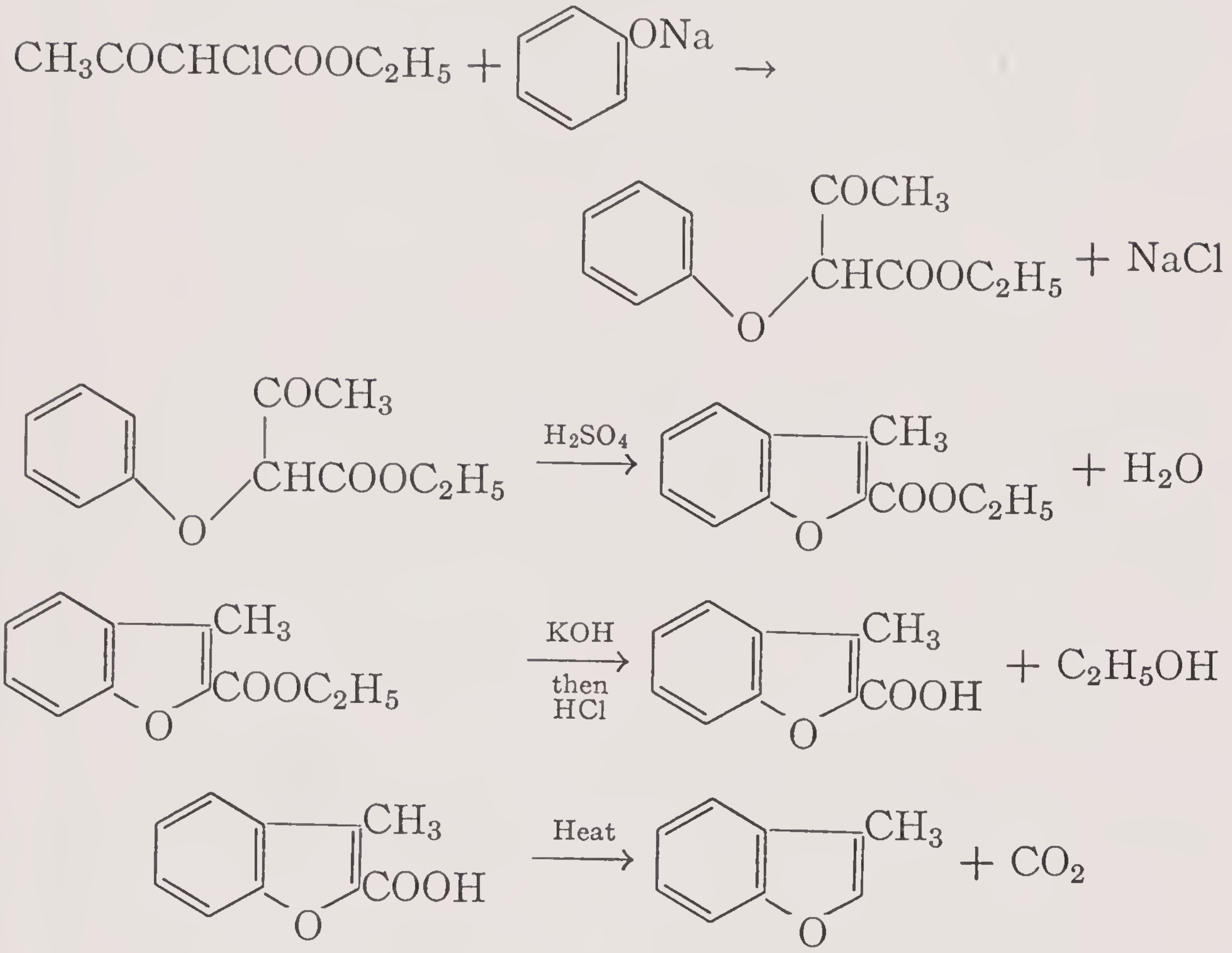
[3] See also *Org. Syntheses* Coll. Vol. **2**, 369 (1943).

[4] Petri, *Ber.*, **14**, 1635 (1881).

3-METHYLCOUMARONE

(Benzofuran, 3-methyl-)

$$CH_3COCH_2COOC_2H_5 + SO_2Cl_2 \rightarrow CH_3COCHClCOOC_2H_5 + HCl + SO_2$$


CH₃COCHClCOOC₂H₅ +
ONa
COCH₃
CHCOOC₂H₅
O
+ NaCl
H₂SO₄
CH₃
COOC₂H₅
+ H₂O
KOH
then
HCl
COOH
+ C₂H₅OH
Heat
+ CO₂

Submitted by WERNER R. BOEHME.[1]
Checked by JAMES CASON and KENNETH L. RINEHART.

1. Procedure

A. *Ethyl 3-methylcoumarilate.* Dry sodium phenolate (116 g., 1 mole) (Note 1) and 1 l. of dry thiophene-free benzene (Note 2) are placed in a 2-l. three-necked flask fitted with mechanical stirrer, dropping funnel, and reflux condenser with drying tube. The suspension is heated to the boiling point on the steam bath, heating is moderated, and 165 g. (1 mole) of ethyl α-chloroacetoacetate (Note 3) is added with stirring through the dropping funnel at such a rate as to maintain gentle refluxing (Note 4). Refluxing and stirring are continued on the steam bath for 4 hours after the addition of the chloroester is completed. The light-brown suspension is cooled to room temperature, extracted with two 500-ml. portions of water, and dried superficially by filtration through a layer of anhydrous magnesium sulfate. The solvent is removed by distillation on the steam bath under water-aspirator vacuum. The brown oil remaining consists of crude ethyl α-phenoxyacetoacetate and weighs 188–200 g. (85–90%).

Concentrated sulfuric acid (195 ml.) is placed in a 2-l. three-necked flask immersed in an ice-salt bath and fitted with a dropping funnel, a thermometer, and a mechanical stirrer. Ethyl α-phenoxyacetoacetate (195 g.) is added with stirring through the dropping funnel as the temperature within the flask is maintained below 5°. About 1 hour is required for the addition. The mixture, which solidifies soon after all the ester has been added, is allowed to stand in the ice bath for 1 hour longer. Ice (500 g.) and water (500 ml.) are added with stirring and external cooling. The mixture is then extracted with two 250-ml. portions of benzene. The combined extracts are washed with 100 ml. of water, then with 100 ml. of saturated aqueous sodium bicarbonate solution, and finally are dried superficially by filtration through a layer of anhydrous magnesium sulfate. The solvent is distilled from the dried extracts, and the residue is fractionated under reduced pressure from a 250-ml. Claisen flask fitted with a short air condenser. The pale yellow oil boils at 162–167°/16 mm. and solidifies on cooling. The product is triturated with a little petroleum ether (b.p. 35–60°) and dried at room temperature. The almost colorless rhombic plates, melting at 49–51°, weigh 60–75 g. (35–42%).

B. *3-Methylcoumarilic acid.* Ethyl 3-methylcoumarilate (70 g.) and 500 ml. of 10% aqueous potassium hydroxide solution are refluxed for 1 hour. The clear yellowish solution is acidified while hot (Note 5) with a slight excess of concentrated hydrochloric acid to precipitate the 3-methylcoumarilic acid. The suspension is cooled to room temperature, and the colorless solid is filtered with suction. The filter cake is resuspended in 500 ml.

of cold water, stirred vigorously for several minutes, and filtered again with suction. The colorless powder, after being dried in a desiccator under reduced pressure, weighs 54–57 g. (90–95%) and melts at 192–193°.

C. *3-Methylcoumarone.* Dry 3-methylcoumarilic acid (50 g.) is distilled from a 250-ml. Claisen flask fitted with a long air condenser and immersed in a Wood's metal bath heated slowly to 280°. Carbon dioxide is evolved, and a cloudy liquid distils at 190–220°. The crude product is purified by redistillation through a Vigreux column (Note 6). The clear colorless distillate, weighing 31.5–33 g. (84–88%), boils at 195–197°, n_D^{25} 1.5520.

2. Notes

1. Sodium phenolate may be prepared *in situ* by evaporating molar equivalents of phenol and sodium hydroxide solution in the reaction flask on the steam bath under reduced pressure and drying the residue by heating the flask for several hours longer on the steam bath under reduced pressure. The solid cake of dry sodium phenolate breaks up in the succeeding step of the synthesis.

2. Benzene is conveniently dried by slowly distilling about 20% of it and cooling the residue with protection from atmospheric moisture by use of a calcium chloride tube.

3. Ethyl α-chloroacetoacetate is prepared by the general method of Allihn.[2] Since the substance is a severe lachrymator and gases evolved during the preparation are difficult to absorb, the entire preparation should be carried out in a hood. In a 1-l. three-necked flask fitted with dropping funnel, a thermometer, and a mechanical stirrer, and connected to a gas-absorption trap,[3] is placed 260 g. (2 moles) technical ethyl acetoacetate. Sulfuryl chloride (270 g., 2 moles) is added slowly with stirring and external cooling, the temperature being maintained between 0° and 5°. About 3 hours is required for the addition. The solution is allowed to stand overnight at room temperature, and hydrogen chloride and sulfur dioxide are removed at 40–50° under water-aspirator vacuum. The residual dark amber liquid is distilled

through a short Vigreux column at reduced pressure. After a small fore-run, the ethyl α-chloroacetoacetate distils at 85–89°/17 mm. The yield of colorless liquid is 308–321 g. (93–97%). The checkers, using a 12-cm. unheated Vigreux column, obtained this yield only after redistilling the combined fore-run and after-run. Ethyl α-chloroacetoacetate is currently available from Distillation Products Industries, Rochester, New York, but it is rather expensive.

4. The time of addition is 20–30 minutes. Some external heating is usually necessary to maintain reflux during the addition.

5. If the solution is allowed to cool much below 70° the potassium salt of 3-methylcoumarilic acid crystallizes in the form of colorless needles.

6. The checkers used an 18-in. Podbielniak column with simple wire spiral, heated jacket, and partial-reflux head.

3. Methods of Preparation

3-Methylcoumarone has been prepared by the cyclization of ethyl α-phenoxyacetoacetate followed by hydrolysis and decarboxylation of the resulting ethyl 3-methylcoumarilate,[4] by debromination and rearrangement of 3,4-dibromo-4-methylcoumarin to 3-methylcoumarilic acid followed by decarboxylation,[4, 5] by cyclization of phenoxyacetone with concentrated sulfuric acid,[6] and by treatment of 3-coumaranone with methylmagnesium iodide followed by dehydration of the resulting carbinol.[7]

The procedure described is a modification of the method of Hantzsch.[4]

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[1] The National Drug Company, Philadelphia, Pennsylvania.

[2] Allihn, *Ber.*, **11**, 567 (1878).

[3] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

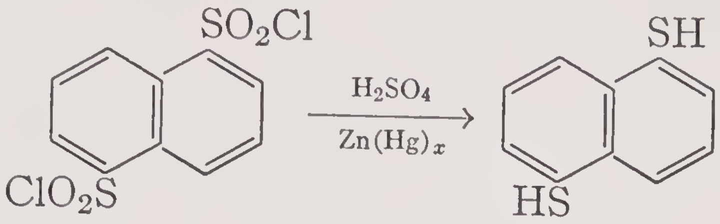
[4] Hantzsch, *Ber.*, **19**, 1290 (1886).

[5] Peters and Simonis, *Ber.*, **41**, 832 (1908).

[6] Stoermer, *Ber.*, **28**, 1254 (1895).

[7] Stoermer and Barthelmes, *Ber.*, **48**, 67 (1915).

1,5-NAPHTHALENEDITHIOL



Submitted by P. D. Caesar.[1]
Checked by Richard T. Arnold, W. E. Parham, and R. M. Scribner.

1. Procedure

A 2-l. round-bottomed flask having standard-taper, ground-glass fittings is equipped with a bulb condenser (Note 1) and an efficient Hershberg stirrer. To this are added with stirring 600 g. (2.0 moles) of 33% sulfuric acid, 20 g. (0.06 mole) of finely divided 1,5-naphthalenedisulfonyl chloride,[2] and 100 g. (1.5 gram atoms) of zinc dust amalgam (Note 2) at room temperature (Note 3). The zinc dust amalgam is added directly after the disulfonyl chloride in the course of 2–5 minutes. The mixture is heated to reflux, held there for about 6 hours, and allowed to cool overnight without agitation (Note 4).

The product is filtered, and the precipitate is extracted with a total of 1 l. of warm ether (Note 5). The combined ether extracts are evaporated to a volume of 50 ml., cooled, and filtered. The filtrate is further evaporated to a volume of about 10 ml., cooled, and again filtered. The precipitates melt at 119–121° and total 7.1–9.1 g. This represents a yield of 60–80%.

The 1,5-naphthalenedithiol can be further purified to a melting point of 120–121° by sublimation under high vacuum in a molecular still, followed by reprecipitation of the water-soluble disodium salt of the sublimate from excess hydrochloric acid. The pure compound obtained from 9.1 g. of product weighs 8.6 g. (76%).

2. Notes

1. The product collects in the condenser, and it may be necessary to clear the condenser with a glass rod.

2. A good grade of zinc and mercury (II) chloride should be used. The zinc dust amalgam is prepared by dissolving 20 g. of mercury (II) chloride in a solution of 10 ml. of concentrated hydrochloric acid in 300 ml. of distilled water, and adding quickly, with stirring, 100 g. of zinc dust (Schaar chemicals, 95% purity). After 10–15 minutes of stirring and crushing lumps, the mixture is filtered through a Büchner funnel, and the zinc dust amalgam is carefully washed with a total of 500 ml. of distilled water containing a trace of hydrochloric acid. The water is then removed by ethanol, the ethanol by ether, and most of the ether by air. It is advisable to remove the zinc dust amalgam from the Büchner funnel and add it to the reduction mixture before all the ether is removed to assure minimum contact with the air.

An occasional batch of zinc dust failed to effect the desired reduction, possibly because of excessive oxide deposition on the surface of the zinc. It is suggested, therefore, that the surface of the zinc dust be cleaned with dilute hydrochloric acid just before amalgamation.

3. This technique eliminates the long induction period at 0° and the violent foaming described in the preparation of thiophenol.[3] However, in a larger-scale operation it would be advisable to check the rate of addition of the zinc dust somewhat, lest an exception arise.

4. The overnight period was a matter of convenience and is not considered to be vital to the completeness of the reaction.

5. When unamalgamated zinc dust is used, a considerable proportion of yellow insoluble product is often noted at this point. Since the disulfide has been isolated as an intermediate in a similar reduction of *m*-chlorosulfonylbenzoic acid,[4] it is probable that this material is a mixture of disulfides of varying molecular weight.

3. Application

This method has been applied successfully to the preparation of phenoxybenzene-4,4′-dithiol (84% of the theoretical amount), diphenylmethane-4,4′-dithiol, and *m*-sulfhydrylbenzoic acid[4] (80%). It did not prove satisfactory for the preparation of higher-melting thiols of lower solubility, such as 2,7-naphthalenedithiol, 2,6-naphthalenedithiol, and 4,4′-biphenyldithiol. These were better prepared by the use of tin (II) chloride 2-hydrate in glacial acetic acid saturated with hydrogen chloride.[5]

4. Methods of Preparation

1,5-Naphthalenedithiol can be prepared by adding 1,5-naphthalenedisulfonyl chloride to an ethanol solution of tin (II) chloride 2-hydrate saturated with hydrogen chloride.[6] An 80% yield of the crude dithiol melting at 103° was previously reported using zinc dust and sulfuric acid.[7]

[1] University of Illinois, Urbana, Illinois.

[2] *Org. Syntheses*, **32**, 88 (1952).

[3] *Org. Syntheses* Coll. Vol. **1**, 504 (1941).

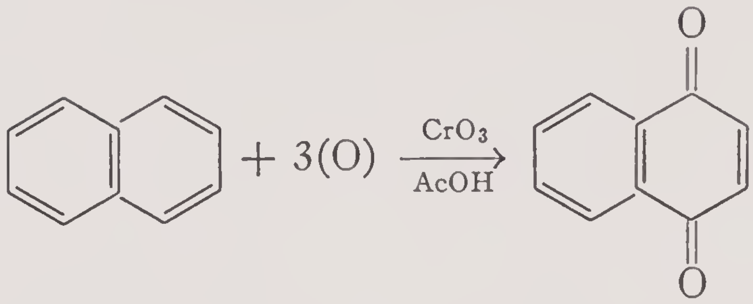
[4] Tennyson, private communication.

[5] Marvel and Caesar, *J. Am. Chem. Soc.*, **73**, 1097 (1951).

[6] Corbellini and Albenga, *Gazz. chim. ital.*, **61**, 111 (1931).

[7] Braun and Ebert, *Ber.*, **25**, 2735 (1892).

1,4-NAPHTHOQUINONE



Submitted by E. A. Braude and J. S. Fawcett.[1]
Checked by Charles C. Price, R. S. Schreiber, R. D. Birkenmeyer, Paul F. Kirk, and William Bradley Reid, Jr.

1. Procedure

In a 2-l. three-necked flask, fitted with a mechanical stirrer, a 1-l. dropping funnel, and a thermometer, is placed a solution of 120 g. (1.2 moles) of pure chromium trioxide (Note 1) in 150 ml. of 80% aqueous acetic acid. The flask is surrounded by a freezing mixture of ice and salt, and, when the temperature of the contents of the flask has fallen to 0°, a solution of 64 g. (0.5 mole) of naphthalene in 600 ml. of glacial acetic acid is gradually added, with constant stirring, over a period of 2–3 hours. The internal temperature is maintained at about 10–15°. Stirring is continued overnight, during which time the reaction mixture and cooling bath gradually attain room temperature (Note 2). The dark green solution is then set aside for 3 days and occasionally stirred.

The crude naphthoquinone is precipitated by pouring the reaction mixture into 6 l. of water. The yellow precipitate is filtered, washed with 200 ml. of water, and dried in a desiccator. The product can be crystallized from 500 ml. of petroleum ether (b.p. 80–100°) (Note 3) and separates in the form of long yellow needles, m.p. 124–125°. The yield is 14–17 g. (18–22%) (Note 4).

2. Notes

1. An equivalent quantity of technical chromium trioxide, ground to a fine powder, may be employed.

2. It is necessary to continue vigorous stirring at this stage in order to prevent local overheating and to keep the mixture from setting to a solid mass.

3. Crystallization from petroleum ether (b.p. 80–100°) is far more convenient than steam distillation as a method of purification, and a product of high purity is obtained after a single crystallization. The checkers used Skellysolve C (b.p. 88–115°) with consistent results. Crystallization from ether has also been employed.[2]

4. The yield is substantially unchanged on increasing the proportion of chromium trioxide used in the oxidation. The submitters report consistent yields of 25–28 g. (32–35%).

3. Methods of Preparation

The present method of preparation is adapted from Miller.[3] Although the yield is relatively low, the method is less costly and time-consuming than those starting from α-naphthol [2] or 1,4-benzoquinone.[4] Other methods that have been employed include the oxidation of naphthalene with hydrogen peroxide,[5] the oxidation of 1,4-naphthalenediamine [6] and naphthylamine sulfonic acid [7] and the oxidation of 4-amino-1-naphthol prepared by electrolytic reduction of 1-nitronaphthalene.[8]

[1] Imperial College of Science and Technology, London, England.

[2] Conant and Fieser, *J. Am. Chem. Soc.*, **46**, 1862 (1924); Fieser and Fieser, *J. Am. Chem. Soc.*, **57**, 491 (1935); *Org. Syntheses* Coll. Vol. **1**, 383 (1946).

[3] Miller, *J. Russ. Phys. Chem. Soc.*, **16**, 414 (1884); cf. Japp and Miller, *J. Chem. Soc.*, **39**, 220 (1881).

[4] Fieser, *J. Am. Chem. Soc.*, **70**, 3165 (1948).

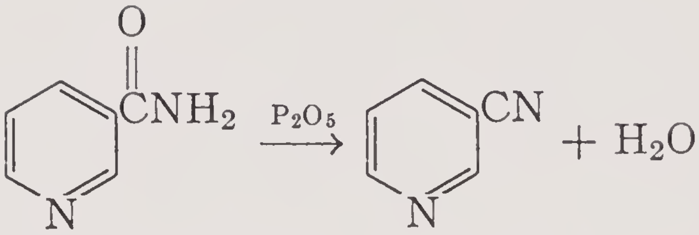
[5] Arnold and Larson, *J. Org. Chem.*, **5**, 250 (1940).

[6] Liebermann, *Ann.*, **183**, 242 (1876); Russig, *J. prakt. Chem.*, **62**, 31 (1900).

[7] Monnet, Reverdin, and Nolting, *Ber.*, **12**, 2306 (1879).

[8] Harman and Cason, *J. Org. Chem.*, **17**, 1058 (1952).

NICOTINONITRILE



Submitted by Peyton C. Teague and William A. Short.[1]
Checked by Arthur C. Cope, John C. Sheehan, and Louis A. Cohen.

1. Procedure

In a dry 1-l. round-bottomed flask are placed 100 g. (0.82 mole) of powdered nicotinamide and 100 g. (0.70 mole) of phosphorus pentoxide. The flask is stoppered and shaken to mix the two powders. It is then connected by means of a 10-mm. i.d. tube to an 80-cm. air condenser arranged for distillation. A 125-ml. Claisen flask immersed in an ice-salt bath is used as the receiver (Note 1). The pressure is reduced to 15–20 mm., and the mixture is heated with a large free flame of a high-temperature burner (such as a Fisher or Meker type). The flame is moved about freely to melt the material as rapidly as possible, and then the mixture is heated vigorously until nothing more comes over or until foam reaches the top of the flask (15–20 minutes). The apparatus is allowed to cool (Note 2), and the product is rinsed out of the tube and condenser with ether (Note 3). The ether solution is added to the distillate, the ether is distilled on a steam bath, and the product is distilled at atmospheric pressure using an air condenser. The yield of nicotinonitrile, boiling at 205–208° and melting at 50–51°, is 71–72 g. (83–84%).

2. Notes

1. To prevent possible clogging of the condenser by the solid nicotinonitrile, the end of the condenser should not be constricted and should not extend far into the receiver.

2. The residue left in the flask may be removed by carefully adding water, allowing the mixture to stand overnight, and then washing repeatedly with water.

3. A small amount of material insoluble in ether but soluble in water remains in the condenser. The nicotinonitrile can be washed from the condenser more easily with acetone. If acetone is used, it should be removed by distillation under reduced pressure before the product is distilled.

3. Methods of Preparation

The method described is essentially that of La Forge.[2] Nicotinonitrile has also been prepared from nicotinic acid by heating with ammonium acetate and acetic acid,[3] from 3-pyridinesulfonic acid by fusion of the sodium salt with sodium cyanide,[4] and from 3-bromopyridine and cuprous cyanide.[5]

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[1] University of South Carolina, Columbia, South Carolina.

[2] La Forge, *J. Am. Chem. Soc.*, **50**, 2477 (1928).

[3] Adkins, Wolff, Pavlic, and Hutchinson, *J. Am. Chem. Soc.*, **66**, 1293 (1944).

[4] McElvain and Goese, *J. Am. Chem. Soc.*, **65**, 2233 (1943).

[5] McElvain and Goese, *J. Am. Chem. Soc.*, **63**, 2283 (1941).

m-NITROBENZAZIDE

(Benzoyl azide, *m*-nitro-)

$$m\text{-}NO_2C_6H_4CO_2H + SOCl_2 \rightarrow m\text{-}NO_2C_6H_4COCl + SO_2 + HCl$$

$$m\text{-}NO_2C_6H_4COCl + NaN_3 \rightarrow m\text{-}NO_2C_6H_4CON_3 + NaCl$$

Submitted by Jon Munch-Petersen.[1]
Checked by William S. Johnson and W. David Wood.

1. Procedure

A. *m-Nitrobenzoyl chloride.* In a 1-l. round-bottomed flask are placed 200 g. (1.2 moles) of crude *m*-nitrobenzoic acid [2] and 500 g. (300 ml., 4.2 moles) of thionyl choride (Note 1). The flask is fitted (ground-glass joint) with a reflux condenser carrying a calcium chloride drying tube leading to a gas-absorption trap[3] and is heated on a steam bath for 3 hours. The condenser is then set for downward distillation, and as much of the excess thionyl chloride as possible is distilled at the temperature of the steam bath. The residue is transferred to a 250-ml. Claisen flask and distilled at reduced pressure (water pump), b.p. 153–154°/12 mm. (Note 2). The yield is 200–217 g. (90–98%), m.p. 33°.

B. *m-Nitrobenzazide.* In a 2-l. round-bottomed flask fitted with an efficient mechanical stirrer is placed a solution of 78 g. (1.2 moles) of commercial sodium azide in 500 ml. of water (Note 3). The flask is surrounded by a water bath kept at 20–25°. The stirrer is started, and over a period of about 1 hour a solution of 185.5 g. (1 mole) of *m*-nitrobenzoyl chloride in 300 ml. of acetone (previously dried over anhydrous potassium carbonate) is added from a dropping funnel. *m*-Nitrobenzazide separates at once as a white precipitate. Stirring is continued for 30 minutes after the addition is complete; then 500 ml. of water is added and the reaction mixture stirred for an additional 30 minutes. The azide is separated on a suction filter, washed with water, and dried in the air. The yield of crude product, m.p. 68°, is 189 g. (98%) (Note 4). It may be recrystallized from a mixture of equal parts of benzene and ligroin (b.p. 100–140°), when the temperature is kept below 50° (Note 5). The product thus obtained consists of almost colorless crystals, m.p. 68–69° (Note 6), the recovery being 80–90% (Note 7).

2. Notes

1. Eastman Kodak Company white-label thionyl chloride is satisfactory.

2. Since the product crystallizes readily, water cooling should be applied only at the receiver, not at the side arm.

3. The reaction should preferably be carried out in a hood, as hydrazoic acid may be liberated in small amounts. This compound, which is volatile, is highly toxic, and its inhalation may cause temporary headache and giddiness.

4. This product is sufficiently pure for general reagent use.

m-Nitrobenzazide is recommended [4–7] as a reagent for the characterization and estimation of aliphatic and aromatic hydroxyl compounds. It reacts to form nicely crystalline *m*-nitrophenylcarbamic esters,[5,6,8] in which the nitro group may be titrated with titanous chloride. With amines it forms substituted *m*-nitrophenylureas.[9,10]

5. At higher temperatures a Curtius rearrangement into the isocyanate may occur, nitrogen being liberated. An alternative procedure for recrystallization (preferred by the checkers) consists in dissolving the crude product in a small amount of benzene (if the solution is discolored it may be treated with decolorizing carbon), and adding an equal volume of ligroin. On seeding, the product crystallizes.

6. The melted compound decomposes with liberation of nitrogen.

7. Using the same procedure, *p*-nitrobenzazide, m.p. 71–72° (Note 6), may be prepared. The yield of crude product is 90%, and of recrystallized product 70%.

3. Methods of Preparation

m-Nitrobenzazide has been prepared by the action of nitrous acid on *m*-nitrobenzhydrazide, which is obtained by treating methyl *m*-nitrobenzoate with hydrazine hydrate.[5,7] The procedure described here is mentioned by Naegeli and Tyabji [11] and is similar to that given for benzazide.[12]

[1] Department of Organic Chemistry, Technical University of Denmark, Copenhagen, Denmark.

[2] *Org. Syntheses* Coll. Vol. **1**, 391 (1941).

[3] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[4] Veibel, *Anal. Chem.*, **23**, 665 (1951).

[5] Sah and Woo, *Rec. trav. chim.*, **58**, 1013 (1939).

[6] Veibel and Lillelund, *Dansk Tidsskr. Farm.*, **14**, 236 (1940) [*C. A.*, **35**, 2444 (1941)].

[7] Veibel, Lillelund, and Wangel, *Dansk Tidsskr. Farm.*, **17**, 183 (1943) [*C. A.*, **39**, 1608 (1945)].

[8] Hoeke, *Rec. trav. chim.*, **54**, 505 (1935).

[9] Sah et al., *J. Chinese Chem. Soc.*, **13**, 22 (1946) [*C. A.*, **42**, 148 (1948)].

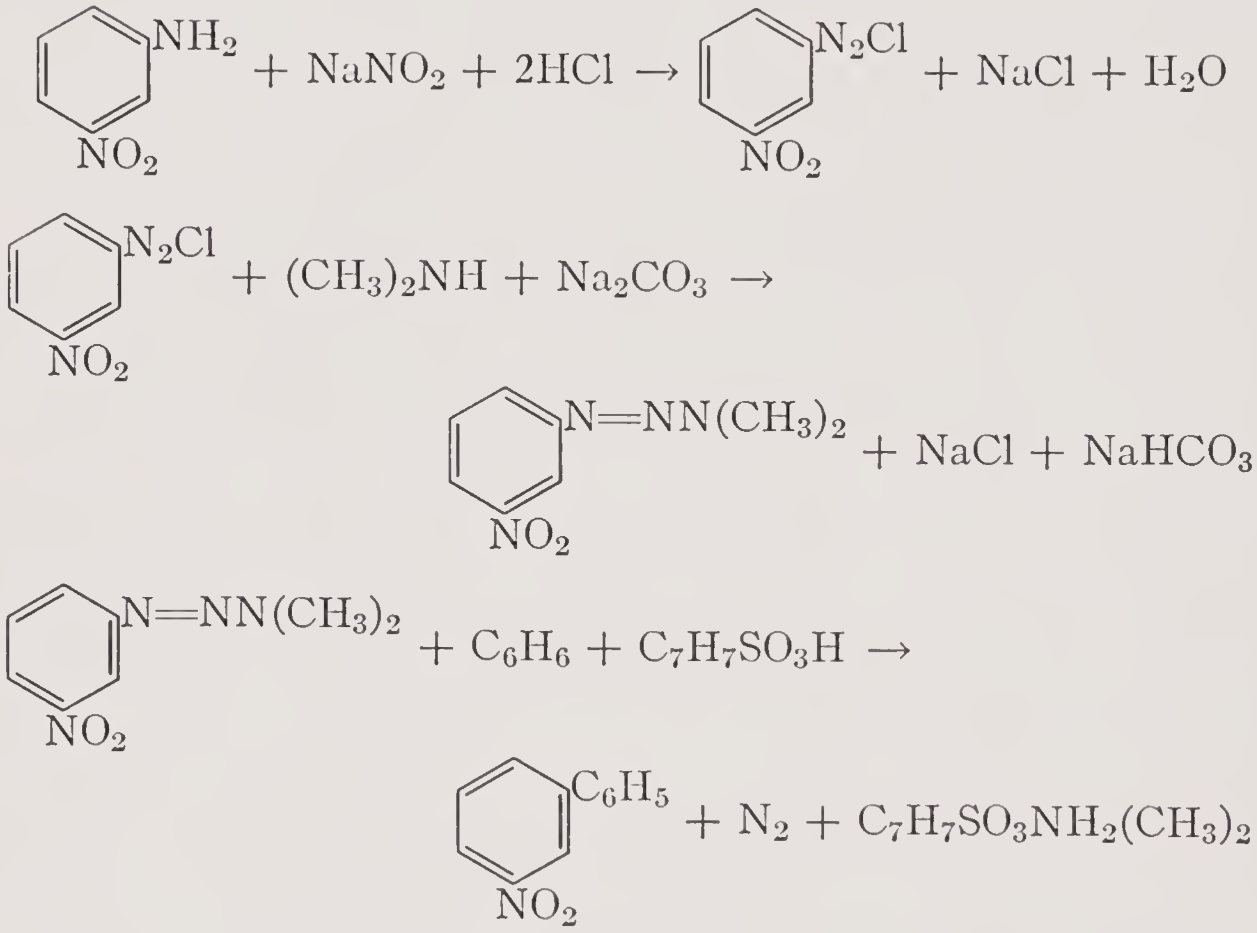
[10] Karrman, *Svensk Kem. Tidskr.*, **60**, 61 (1948) [*C. A.*, **42**, 5804 (1948)].

[11] Naegeli and Tyabji, *Helv. Chim. Acta*, **16**, 361 (1933).

[12] Barret and Porter, *J. Am. Chem. Soc.*, **63**, 3434 (1941).

m-NITROBIPHENYL

(Biphenyl, 3-nitro-)


NH₂
+ NaNO₂ + 2HCl →
N₂Cl
+ NaCl + H₂O
NO₂
NO₂
N₂Cl
+ (CH₃)₂NH + Na₂CO₃ →
NO₂
N=NN(CH₃)₂
+ NaCl + NaHCO₃
NO₂
N=NN(CH₃)₂
+ C₆H₆ + C₇H₇SO₃H →
NO₂
C₆H₅
+ N₂ + C₇H₇SO₃NH₂(CH₃)₂
NO₂

Submitted by C. E. Kaslow and R. M. Summers.[1]
Checked by James Cason and B. H. Walker.

1. Procedure

A. *1-(m-Nitrophenyl)-3,3-dimethyltriazene.* To a 3-l. three-necked flask containing 276 g. (2 moles) of technical grade *m*-nitroaniline (Note 1) are added 250 ml. of concentrated hydrochloric acid and 500 ml. of hot water. The contents of the flask are heated to about 85° to dissolve the *m*-nitroaniline; then 550 ml. of concentrated hydrochloric acid is added, and the solution is cooled rapidly. A stirrer, a thermometer, and a long-stemmed dropping funnel are attached to the flask, and its contents are then cooled to −3 to −5° by means of a salt-ice bath. A solution of 144 g. (2.09 moles) of sodium nitrite in 350 ml. of water is added dropwise under the surface of the acid solution while it is being stirred. The rate of addition is regulated (Note 2) so that the temperature does not rise above 0°. The stirring is continued for 15–20 minutes after the sodium nitrite solution has been added; then a solution of 8–10 g. of urea in 25 ml. of water is added during about 15 minutes (foaming), and the stirring is discontinued. The diazonium salt solution must be kept cold while the next step is proceeding.

Two and one-half liters of water in a 3-gal. crock is stirred vigorously with a mechanical stirrer, and 870 g. (7 moles) of pulverized sodium carbonate monohydrate (Note 3) is added portionwise (Note 4). Crushed ice is added to the sodium carbonate suspension until the temperature is lowered to 10°; then 423 g. (2.35 moles) of 25% dimethylamine solution (Note 5) is added. The ice-cold *m*-nitrobenzenediazonium chloride solution is added over a period of 25–35 minutes under the surface of the vigorously stirred dimethylamine solution by means of a dropping funnel (Note 6) while the temperature is maintained at about 10° by the addition of ice. The solution is stirred for 15–20 minutes after the addition is complete. The crude yellow triazene is removed by filtration on a large Büchner funnel. The cake is washed twice by removal and thorough mixing with 2–2.5 l. of water. After the second washing the cake is pressed as dry as possible, then removed and dissolved in 1.8–2.0 l. of boiling 95% ethanol contained in a 4-l. flask under a reflux condenser. The triazene is allowed to crystallize as the ethanol is cooled in water, then removed by filtration, and washed with two 200-ml. portions of 95% ethanol. After drying in air at room temperature, the yield of 1-(*m*-nitrophenyl)-3,3-dimethyltriazene is 348–365 g. (89–94%), m.p. 100.8–101.5°.

B. *m-Nitrobiphenyl.* To a 5-l. three-necked flask equipped with a sealed mechanical stirrer, a dropping funnel, and a reflux condenser are added 116.4 g. (0.6 mole) of 1-(*m*-nitrophenyl)-3,3-dimethyltriazene and 2.5 l. of benzene. The benzene solution is heated to maintain refluxing and stirred vigorously while a solution of 148 g. (0.8 mole) of 94% toluenesulfonic acid (Note 7) in 750 ml. of benzene is added dropwise (Note 8) over a period of 4–4.5 hours. The refluxing is continued for 1–1.5 hours (Note 9) after the toluenesulfonic acid has been added. The solution is allowed to cool somewhat, 800 ml. of water is added cautiously with stirring through the separatory funnel, and then the water layer is removed. The benzene layer is extracted twice with 500-ml. portions of water, then three times with 500-ml. portions of 5% sodium hydroxide solution, and finally with a 500-ml. portion of water. The benzene solution is shaken with 30–40 g. of anhydrous calcium chloride to remove most of the water. The benzene is removed by distillation by dripping it into a 500-ml. Claisen flask which is heated sufficiently to maintain a rapid rate of distillation. After most of the benzene is removed, the residue is transferred to a 125-ml. Claisen flask. The low-boiling material is removed at a pressure of 20–30 mm. up to a bath temperature of 135–140°. The residue is then distilled at 0.1 mm. pressure. After a fore-run of nitrobenzene (2–5 ml.), the *m*-nitrobiphenyl is distilled (Note 10) at 115–118° at 0.1 mm. while the bath temperature is maintained at 155–160°. The yield of the crude yellow oil is 50–60 g. (42–50%) (Note 11). For purification, the substance is dissolved in 50 ml. of hot methanol. Upon cooling, two layers separate. Crystallization is induced by scratching the inner surface with a glass rod. When the crystalline mass is cold, the yellow solid is removed by filtration and washed with two 30-ml. portions of cold methanol. After drying in air, the yield of *m*-nitrobiphenyl is 40–50 g. (34–42%), m.p. 58.5–59.5°.

2. Notes

1. E. I. du Pont de Nemours and Company technical product, m.p. 111–112°, was used.

2. The time required for the addition varies from 1.5 to 2 hours.

3. There must be an excess of sodium carbonate to prevent the troublesome frothing caused by the liberation of carbon dioxide near the end of the coupling reaction.

4. The addition must be regulated so as to prevent the formation of large chunks of sodium carbonate decahydrate.

5. Obtained from Eastman Organic Chemicals Department, Distillation Products Industries, Rochester, New York.

6. Small portions are added to the separatory funnel while the main portion is kept in the ice bath.

7. Monsanto Chemical Company anhydrous toluenesulfonic acid, which is about 80% of the *para* isomer, was used.

8. Some toluenesulfonic acid hydrate which does not dissolve in benzene must be pushed through the stem of the funnel by means of a wire or a thin glass rod.

9. The evolution of nitrogen gas may be followed by attaching a bubble counter containing kerosene to the top of the reflux condenser. Generally, the evolution of nitrogen is complete within an hour.

10. The *m*-nitrobiphenyl has a tendency to crystallize in the side arm of the Claisen flask. Arrangements must be made to keep the side arm sufficiently warm to prevent crystallization.

11. After the oil has congealed to a solid, the substance melts at 53–57°.

3. Methods of Preparation

The procedure described for the preparation of 1-(*m*-nitrophenyl)-3,3-dimethyltriazene is the method of Elks and Hey,[2] and the preparation of *m*-nitrobiphenyl is also a modification of their procedure. The other principal methods for the preparation of *m*-nitrobiphenyl are the decomposition of N-nitroso-*m*-nitroacetanilide in benzene [3] and the decomposition of alkaline *m*-nitrobenzenediazohydroxide in benzene.[4] Other methods that have been reported include the decomposition of potassium *m*-nitrobenzenediazotate in benzene with acetyl chloride,[5] the decomposition of *m*-nitrobenzoyl peroxide in boiling benzene,[6] the decomposition of benzenediazonium borofluoride in nitrobenzene [7] at 70°, and the reduction of 4-(3′-nitrophenyl)-benzenediazonium acid sulfate in boiling ethanol.[8]

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[1] Indiana University, Bloomington, Indiana.

[2] Elks and Hey, *J. Chem. Soc.*, **1943**, 441.

[3] Bachmann and Hoffman, in Adams, *Organic Reactions*, Vol. 2, p. 249, John Wiley & Sons, 1944.

[4] Gomberg and Bachmann, *J. Am. Chem. Soc.*, **46**, 2339 (1924); Blakey and Scarborough, *J. Chem. Soc.*, **1927**, 3000; Elks, Haworth, and Hey, *J. Chem. Soc.*, **1940**, 1284.

[5] Jacobsen and Loeb, *Ber.*, **36**, 4082 (1903).

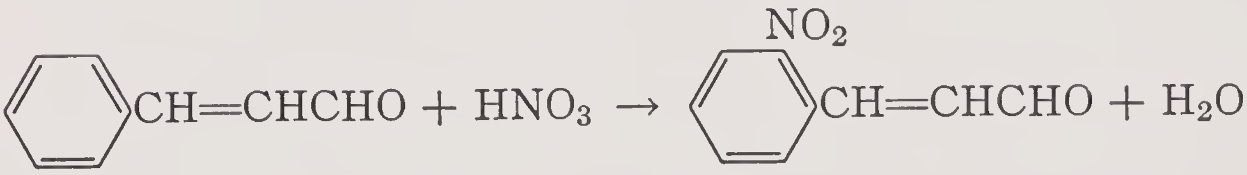
[6] Hey and Walker, *J. Chem. Soc.*, **1948**, 2213.

[7] Nesmeyanov and Makarova, *Bull. acad. sci. U.R.S.S., Classe sci. chim.*, **1947**, 213 [*C. A.*, **42**, 5441*a* (1948)].

[8] Fichter and Sulzberger, *Ber.*, **37**, 878 (1904).

o-NITROCINNAMALDEHYDE

(Cinnamaldehyde, *o*-nitro-)



Submitted by Robert E. Buckles and M. Peter Bellis.[1]
Checked by Richard T. Arnold and James D. Groves.

1. Procedure

A 1-l. three-necked round-bottomed flask, fitted with a dropping funnel and a mechanical stirrer, is cooled in an ice-salt mixture. To the flask are added 55.5 g. (50 ml., 0.42 mole) of freshly distilled cinnamaldehyde (Note 1) and 225 ml. of acetic anhydride. When the temperature of the solution has reached 0–5° a solution of 18 ml. of concentrated nitric acid (sp. gr. 1.42) in 50 ml. of glacial acetic acid is added slowly through the dropping funnel while the mixture is stirred. The time of addition is 3–4 hours, during which the temperature is kept below 5°. After the addition is complete, the mixture is allowed to warm slowly to room temperature. The reaction flask is then dismantled and stoppered, and the reaction mixture is allowed to stand 2 days.

At the end of this time, hydrochloric acid (20%) is added cautiously to the cooled solution until a precipitate begins to appear (Note 2). The addition of acid is then stopped, and the solution is allowed to cool in an ice bath or refrigerator until precipitation of the solid is completed. The light-yellow needles are collected on a Büchner funnel and dried in air. About 24 g. of *o*-nitrocinnamaldehyde, m.p. 125–127°, is obtained (Note 3).

Additional product can be isolated by cautiously adding water to the mother liquor until precipitation is observed and then cooling the resultant mixture for several hours in an ice bath. Recrystallization from 95% ethanol gives 5–10 g. of *o*-nitrocinnamaldehyde, m.p. 126–127°. The total yield is 27–34 g. (36–46%).

2. Notes

1. As with other aromatic aldehydes, cinnamaldehyde is readily oxidized by air to its corresponding carboxylic acid. The latter must be separated just before the use of the aldehyde.

2. A good deal of heat is evolved when the hydrochloric acid is added to the reaction mixture, owing to the hydrolysis of acetic anhydride. The reaction mixture will become excessively hot unless it is cooled in an ice bath.

3. The product obtained is pure enough for most purposes. Recrystallization from 95% ethanol yields a nearly white product, m.p. 126–127.5°.

3. Methods of Preparation

o-Nitrocinnamaldehyde has been prepared by the condensation of *o*-nitrobenzaldehyde with acetaldehyde.[2,3] The direct nitration of cinnamaldehyde with potassium nitrate in sulfuric acid yields *o*-nitrocinnamaldehyde along with *p*-nitrocinnamaldehyde.[3] The nitration of cinnamaldehyde in acetic anhydride yields *o*-nitrocinnamaldehyde as the only product.[4] This procedure is the basis for the one given above.

[1] The State University of Iowa, Iowa City, Iowa.

[2] Baeyer and Drewsen, *Ber.*, **16**, 2205 (1883).

[3] Diehl and Einhorn, *Ber.*, **18**, 2335 (1885).

[4] Mills and Evans, *J. Chem. Soc.*, **117**, 1035 (1920).

m-NITROSTYRENE

(Styrene, m-nitro-)

$$m\text{-}NO_2C_6H_4CHO + CH_2(CO_2H)_2 \xrightarrow{\text{Pyridine}} m\text{-}NO_2C_6H_4CH{=}CHCO_2H + CO_2 + H_2O$$

$$m\text{-}NO_2C_6H_4CH{=}CHCO_2H \xrightarrow[\text{Quinoline}]{\text{Heat, Cu}} m\text{-}NO_2C_6H_4CH{=}CH_2 + CO_2$$

Submitted by Richard H. Wiley and Newton R. Smith.[1]
Checked by Richard T. Arnold, William E. Parham, and Darwin D. Davis.

1. Procedure

A. *m-Nitrocinnamic acid.* In a 1-l. round-bottomed flask fitted with a reflux condenser are placed 151 g. (1 mole) of m-nitrobenzaldehyde (Note 1), 115 g. (1.1 moles) of malonic acid, 250 ml. of 95% ethanol, and 25 ml. of pyridine. The mixture is heated on a steam bath under gentle reflux for 6–8 hours and cooled. The large masses of crystals are broken up with a spatula, and the reaction mixture is cooled in an ice bath. The solid is collected on a Büchner funnel, and the residue is washed with 100 ml. of cold ethanol and then with two 100-ml. portions of diethyl ether. The crude m-nitrocinnamic acid is suspended in 300 ml. of ethanol and digested on a steam plate for 2–3 hours. The mixture is cooled and filtered, and the solid is air-dried. The product, 144–155 g. (75–80%), is a light-yellow solid and melts at 200–201° (Note 2).

B. *m-Nitrostyrene.* In a 250-ml. two-necked flask equipped with a 250° thermometer and an air condenser are placed 30 g. (0.155 mole) of m-nitrocinnamic acid, 2 g. of copper powder, and 60 ml. of dry quinoline (Note 3). The flask is heated with a Bunsen burner to 185–195°, during which time a steady stream of carbon dioxide is evolved. After 2–3 hours (Note 4), the reaction mixture is cooled and poured into a mixture of 75 ml. of concentrated hydrochloric acid and 175 g. of ice. The m-nitrostyrene is isolated by steam distillation, approximately 1 l. of distillate being collected. The aqueous distillate is extracted with three 50-ml. portions of chloroform, which are combined and dried over anhydrous sodium sulfate. A 50-ml. Claisen flask, equipped with a dropping funnel, is heated on a steam bath, and the filtered chloroform extract is added dropwise. Heating is continued until all the solvent has been removed. The residue is then distilled at 3–5 mm. pressure. Following a small fore-run of less than 1 g. (Note 5), the *m*-nitrostyrene distils as a yellow liquid. The yield is 13–14 g. (55–59%), b.p. 90–96°/3.5 mm., n_D^{20} 1.5836, n_D^{27} 1.5800–1.5802 (Notes 6 and 7).

2. Notes

1. The checkers used technical *m*-nitrobenzaldehyde melting at 53–56°.

2. This procedure has been used by the submitters and others to prepare the following cinnamic acids from substituted benzaldehydes: *o*-nitrocinnamic acid (70%),[2] *p*-nitrocinnamic acid (77%),[2] *m*-cyanocinnamic acid (71%),[3] *o*-chlorocinnamic acid (82%),[4] *m*-chlorocinnamic acid (53%),[4] *p*-chlorocinnamic acid (73%),[4] 2,4-dichlorocinnamic acid (70%),[4] 3,4-dichlorocinnamic acid (81%),[4] *m*-bromocinnamic acid (31%),[4] *p*-methoxycinnamic acid (60%),[4] and 3,4-dimethoxycinnamic acid (77%).[4]

The method constitutes a simple preparation of ethanol-insoluble cinnamic acids, of a high degree of purity when compared with the Perkin reaction [5] or the usual procedure for the Doebner reaction,[6] which uses a large excess of pyridine. A useful modification of this reaction is to warm the reactants on a steam plate in the absence of alcohol.[7, 8]

3. Quinoline that has been purified by steam distillation of an acid solution should be used. Crude quinoline sometimes contains non-basic, high-boiling impurities such as nitrobenzene, which make the purification of *m*-nitrostyrene more difficult.

4. The checkers obtained a lower yield (9–11 g.) when a 2-hour heating period was used. The reaction must be carried out at 195° until the evolution of carbon dioxide has practically ceased

(usually 2.75 hours). The checkers used Mallinckrodt copper powder.

5. The checkers obtained essentially no fore-run and only trace amounts of solid residue. The refractive index of the first 200 mg. was n_D^{27} 1.5800; of the center fractions, n_D^{27} 1.5802; and of the last 700 mg., n_D^{27} 1.5800.

6. This procedure has been used in the preparation of other nitrostyrenes in the following yields: *o*-nitrostyrene (40%),[2] *p*-nitrostyrene (41%),[2] and 3-nitro-4-hydroxystyrene (60%).[2] A better procedure for more volatile styrenes involves simultaneous decarboxylation and codistillation with quinoline from the reaction flask. This method has been used to prepare the following styrenes: *o*-chlorostyrene (50%),[4] *m*-chlorostyrene (65%),[4] *p*-chlorostyrene (51%),[4] *m*-bromostyrene (47%),[4] *o*-methoxystyrene (40%),[4] *p*-methoxystyrene (76%),[4] *m*-cyanostyrene (51%),[3] and *p*-formylstyrene (52%).[9]

7. Larger runs usually give smaller percentage yields.

3. Methods of Preparation

m-Nitrocinnamic acid has been prepared from *m*-nitrobenzaldehyde with sodium acetate and acetic anhydride,[5] and by the condensation of *m*-nitrobenzaldehyde with malonic acid in the presence of bases.[8, 10]

m-Nitrostyrene has been prepared by boiling the sodium salt of β-bromo-β-(*m*-nitrophenyl)-propionic acid,[11] by the dehydration of *m*-nitrophenylmethylcarbinol with phosphorus pentoxide [12] and potassium bisulfate,[13] and by the decarboxylation of *m*-nitrocinnamic acid.[14]

[1] University of Louisville, Louisville, Kentucky.

[2] Wiley and Smith, *J. Am. Chem. Soc.*, **72**, 5198 (1950).

[3] Wiley and Smith, *J. Am. Chem. Soc.*, **70**, 1560 (1948).

[4] Walling and Wolfstirn, *J. Am. Chem. Soc.*, **69**, 852 (1947).

[5] Schiff, *Ber.*, **11**, 1783 (1878); Tiemann and Oppermann, *Ber.*, **13**, 2060 (1880); Reoch and Koehler, *Ber.*, **46**, 3732 (1913); Posner, *J. prakt. Chem.*, [2] **82**, 425 (1910); Boch, Lock, and Schmidt, *Monatsh.*, **64**, 408 (1934); *Org. Syntheses* Coll. Vol. **1**, 398 (1941).

[6] *Org. Syntheses*, **31**, 35 (1951).

[7] Pandya, Ittyerah, and Pandya, *J. Univ. Bombay*, **10**, pt. 3, 78 (1941); Pandya and Pandya, *Proc. Indian Acad. Sci.*, **14A**, 112 (1941).

[8] Dutt, *Quart. J. Indian Chem. Soc.*, **1**, 297 (1925); Kurien, Pandya, and Surange, *Quart. J. Indian Chem. Soc.*, **11**, 824 (1934).

[9] Wiley and Hobson, *J. Am. Chem. Soc.*, **71**, 2429 (1949).

[10] Knoevenagel, *Ber.*, **31**, 2610 (1898).

[11] Prausnitz, *Ber.*, **17**, 597 (1884).

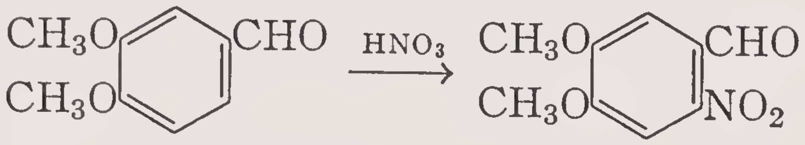
[12] Marvel, Overberger, Allen, and Saunders, *J. Am. Chem. Soc.*, **68**, 736 (1946).

[13] Matsui, *J. Soc. Chem. Ind. Japan*, **45** (supplementary binding), 437 (1942).

[14] Wiley and Smith, *J. Am. Chem. Soc.*, **70**, 2295 (1948).

6-NITROVERATRALDEHYDE

(Veratraldehyde, 6-nitro-)



Submitted by Charles A. Fletscher.[1]
Checked by Richard T. Arnold, W. E. Parham, and Donald A. Leister.

1. Procedure

The product of this reaction is quite sensitive to light, and the entire procedure should be carried out in semidarkness (Note 1).

A wide-mouth 1-l. Erlenmeyer flask is supported inside a water bath of at least 2-l. capacity so that the bottom of the flask is not in contact with the bottom of the bath. The bath is filled with water at about 15° to cover at least half the height of the flask. The flask is fitted with a moderate-speed stainless-steel propeller-type stirrer, and 350 ml. of nitric acid (sp. gr. 1.4) at 20° is poured into it. Veratraldehyde,[2] 70 g. (0.42 mole) (Note 2), is crushed at least as fine as rice grains and is slowly added in small portions to the acid. The rate of addition should be such that it requires about 1 hour to add all the aldehyde. It is helpful, although not usually necessary, to add two or three ice cubes to the bath at the start of the nitration. The internal temperature is checked from time to time and should be held between 18°

and 22°. The mixture is stirred for 10 minutes after the addition of the last of the aldehyde.

The mixture is then poured into 4 l. of vigorously agitated cold water (Note 3) in a suitable opaque container. From this point onward the protection of the product from light is extremely important. The stirring is continued for a few minutes; then the batch is filtered through a 24-cm. Büchner funnel. The container and funnel are kept covered with an opaque sheet of some kind except while the transfer is being made. The cake is sucked down well and then returned to the crock and reslurried a few minutes with 2 l. of cold water. It is then refiltered, pressed out well with a spatula, and drained as well as possible.

The filter cake at this point is 60% to 80% water, and the material is sensitive to heat and to light. The drying, therefore, is difficult and slow, and the exact procedure will depend upon the equipment available. One satisfactory method is to set the Büchner funnel containing the wet material in a large forced-draft oven for 8 hours at 50°. The material, still very wet, is then easily spread on a tray and is placed in a dark but ventilated storeroom, where it is allowed to air-dry for 48 hours or until the weight of the product is less than about 90 g. The product now contains from 10% to 20% of water and is best recrystallized without more thorough drying.

The material is dissolved in 2 l. of boiling 95% ethanol. It is not necessary to filter this solution for the first crystallization. Upon standing overnight, the solution is solid with precipitate. This structure is easily broken up and is filtered on a large Büchner. The mother liquor is concentrated to about 700 ml. and allowed to cool. The second crop of solid is added to the first and dried in a vacuum oven at 50° overnight. The dry material weighs 65–70 g., corresponding to a yield of 73–79%, and melts at 129–131°. It is sufficiently pure for most purposes. One additional crystallization from 1 l. of 95% ethanol gives 55–60 g. of pure material, melting at 132–133°.

2. Notes

1. A sample of 6-nitroveratraldehyde of original melting point 133°, after 9 hours' exposure to the diffused light of the laboratory, showed a melting point of 88–95°. A small quantity of 6-nitroveratric acid, m.p. 185–190°, was isolated from the altered material.

2. The veratraldehyde should have a minimum melting point of 43°. Since there is no difficulty in controlling this reaction, larger batches would undoubtedly be as efficient. The phenomenal bulk of the product and the necessity of minimizing exposure to light make it impractical to handle appreciably more at one time. Smaller batches are perfectly feasible, although it is suggested that for very small amounts of aldehyde somewhat more than the proportional quantity of nitric acid be used. It has been found satisfactory to use 100 ml. of acid with 15 g. of aldehyde.

3. If less water is used, the material is more difficult to break up and wash adequately, and the crude material is more heat-sensitive. Very vigorous agitation is desirable during this precipitation.

3. Methods of Preparation

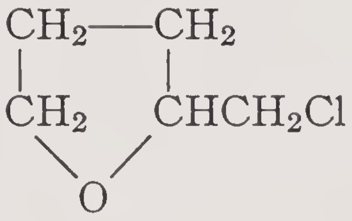
6-Nitroveratraldehyde has always been prepared by direct nitration of the aldehyde. This preparation is a modification of that given by Salway.[3]

[1] Cluett, Peabody and Company, Troy, New York.

[2] *Org. Syntheses* Coll. Vol. 2, 619 (1943).

[3] Salway, *J. Chem. Soc.*, **95**, 1163 (1909).

4-PENTYN-1-OL



$$+ \ 3NaNH_2 \xrightarrow{\text{Liq. } NH_3} NaCl + 3NH_3 + NaC{\equiv}CCH_2CH_2CH_2ONa$$

$$NaC{\equiv}CCH_2CH_2CH_2ONa + 2NH_4Cl \rightarrow 2NaCl + 2NH_3 + HC{\equiv}CCH_2CH_2CH_2OH$$

Submitted by E. R. H. Jones, Geoffrey Eglinton, and M. C. Whiting.[1]
Checked by Arthur C. Cope and Ronald M. Pike.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to ammonia.

A solution of sodium amide in liquid ammonia is prepared according to a procedure previously described (Note 1) in a 3-l. three-necked round-bottomed flask equipped with a cold-finger condenser (cooled with Dry Ice) attached through a soda-lime tower to a gas-absorption trap,[2] a mercury-sealed stirrer, and an inlet tube. Anhydrous liquid ammonia (1 l.) is introduced from a commercial cylinder through the inlet tube, and 1 g. of hydrated ferric nitrate is added, followed by 80.5 g. (3.5 gram atoms) of clean, freshly cut sodium (Notes 1 and 2). The inlet tube is replaced with a 250-ml. dropping funnel, and the mixture is stirred until all the sodium is converted into sodium amide, after which 120.5 g. (1 mole) of tetrahydrofurfuryl chloride[3] (Note 3) is added over a period of 25 to 30 minutes. The mixture is stirred for an additional period of 1 hour, after which 177 g. (3.3 moles) of solid ammonium chloride is added in portions at a rate that permits control of the exothermic reaction. The flask is allowed to stand overnight in the hood while the ammonia evaporates. The residue is extracted thoroughly with ten 250-ml. portions of ether, which are decanted through a Büchner funnel (Note 4). The ether is distilled, and the residue is fractionated at a reflux ratio of about 5 to 1, through a column containing a 20-cm. section packed with glass helices yielding 63–71 g. (75–85%) of 4-pentyn-1-ol, b.p. 70–71°/29 mm., n_D^{25} 1.4443 (Note 5).

2. Notes

1. One of the procedures for converting sodium to sodium amide described in *Organic Syntheses* is used.[4,5]

2. More liquid ammonia should be added through the inlet tube if vaporization reduces the liquid volume to less than 750 ml.

3. Freshly distilled tetrahydrofurfuryl alcohol should be used in the preparation of tetrahydrofurfuryl chloride according to the procedure of *Organic Syntheses*.[3]

4. Ether extraction of the solid must be thorough or the yield will be reduced. A large Soxhlet extractor may be used if desired.

5. Others have reported b.p. 154–155°, n_D^{19} 1.4432;[6] b.p. 154–155°, $n_D^{22.5}$ 1.4450.[7] A sample purified through the silver derivative had b.p. 77°/37 mm., n_D^{15} 1.4464. The α-naphthylurethan of 4-pentyn-1-ol crystallized as needles from 60–80° petroleum ether; m.p. 79–80°.

3. Methods of Preparation

4-Pentyn-1-ol has been prepared from 4-penten-1-ol [3] by bromination followed by dehydrobromination with alkali,[7] by the reaction of 3-bromodihydropyran with *n*-butylsodium or *n*-butyllithium,[6,8] by the reaction of 2-methylenetetrahydrofuran with *n*-amylsodium or *n*-butyllithium,[8] and by the method used in this preparation.[9]

[1] Victoria University of Manchester, Manchester, England.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] *Org. Syntheses*, **25**, 84 (1945).

[4] *Org. Syntheses*, **25**, 25 (1945).

[5] *Org. Syntheses*, **30**, 72 (1950).

[6] Paul and Tchelitcheff, *Compt. rend.*, **230**, 1473 (1950); Paul, *Angew. Chem.*, **63** 304 (1951); Paul, *Bull. soc. chim. France*, **18**, 109 (1951).

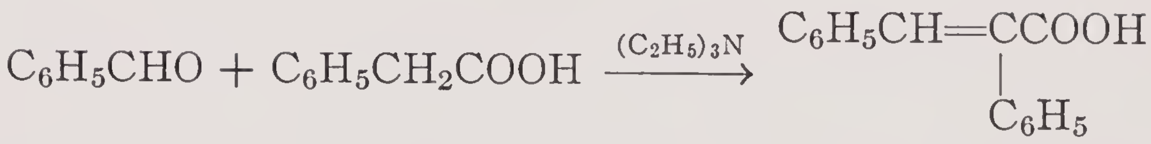
[7] Lespieau, *Compt. rend.*, **194**, 287 (1932).

[8] Paul and Tchelitcheff, *Bull. soc. chim. France*, **19**, 808 (1952).

[9] Eglinton, Jones, and Whiting, *J. Chem. Soc.*, **1952**, 2873.

α-PHENYLCINNAMIC ACID

(Acrylic acid, α,β-diphenyl-)



$$C_6H_5CHO + C_6H_5CH_2COOH \xrightarrow{(C_2H_5)_3N} C_6H_5CH{=}\underset{\underset{\displaystyle C_6H_5}{|}}{C}COOH$$

Submitted by Robert E. Buckles and Keith Bremer.[1]
Checked by T. L. Cairns and J. C. Lorenz.

1. Procedure

In a 500-ml. round-bottomed flask are placed 40.5 ml. (42.4 g., 0.40 mole) of freshly purified benzaldehyde (Note 1), 54.6 g. (0.40 mole) of phenylacetic acid,[2] 40 ml. of anhydrous triethylamine (Note 2), and 80 ml. of acetic anhydride (Note 3). The mixture is boiled gently under reflux for 5 hours. After the heating period is over, the 500-ml. flask containing the reaction mixture is incorporated into a steam-distillation apparatus (Note 4). The reaction mixture is distilled with steam until the distillate coming over is no longer cloudy, and then about 50 ml. more of the distillate is collected. The distillate can be discarded. The aqueous residue is cooled, and the solution is then separated from the solid by decantation. The solid is dissolved in 500 ml. of hot 95% ethanol, and 500 ml. of water, including the solution originally decanted from the crude solid, is added to the hot solution. The mixture is heated to boiling, and 2 g. of decolorizing carbon is added. The hot solution is filtered, and the filtrate is immediately acidified to Congo red with 6 *N* hydrochloric acid. The solution is cooled, and the resulting crystals are removed from the mixture by filtration. The yield of crude α-phenylcinnamic acid (m.p. around 161–165°) is 60–67 g. The product is purified by crystallization from aqueous ethanol (Note 5). The over-all yield of purified product, m.p. 172–173°, is 48–53 g. (54–59%). The product is the isomer with the two phenyl groups *cis* to each other since decarboxylation yields *cis*-stilbene [3] (see p. 88).

2. Notes

1. Benzaldehyde, suitable for this synthesis, is purified in the following way. A 60-g. (58-ml.) sample is washed with two 20-ml. portions of 10% sodium carbonate and then with water. It is then dried over 5–10 g. of anhydrous magnesium sulfate. A few small crystals of hydroquinone or catechol are added with the drying agent. The dry benzaldehyde is decanted through a cotton plug into a Claisen flask; it is distilled under reduced pressure, preferably below 30 mm.

2. Sharples anhydrous grade triethylamine was used without further purification.

3. The acetic anhydride is carefully fractionated; the 137–139° fraction is collected.

4. A simple steam-distillation apparatus such as that given by Fieser [4] is entirely satisfactory. It is usually necessary to heat the distillation flask with a steam bath or a small flame in order to minimize the accumulation of excess water in the flask.

5. The submitters used 5 ml. of 95% ethanol and 5 ml. of water per gram of crude product for recrystallization. The checkers found use of 3:2 ethanol:water by volume more convenient.

3. Methods of Preparation

α-Phenylcinnamic acid has been prepared by the distillation of benzylmandelic acid,[5] by the condensation of phenylacetyl chloride [6] or phenylacetic acid [7] with benzaldehyde in the presence of triethylamine, and by the reaction of sodium or potassium phenylacetate with benzaldehyde in acetic anhydride.[8–11] The most convenient synthesis appears to be that described above.[12, 13]

[1] State University of Iowa, Iowa City, Iowa.

[2] *Org. Syntheses* Coll. Vol. **1**, 436 (1941).

[3] Taylor and Crawford, *J. Chem. Soc.*, **1934**, 1130.

[4] Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 70, D. C. Heath and Company, Boston, 1941.

[5] Malkin and Robinson, *J. Chem. Soc.*, **127**, 376 (1925).

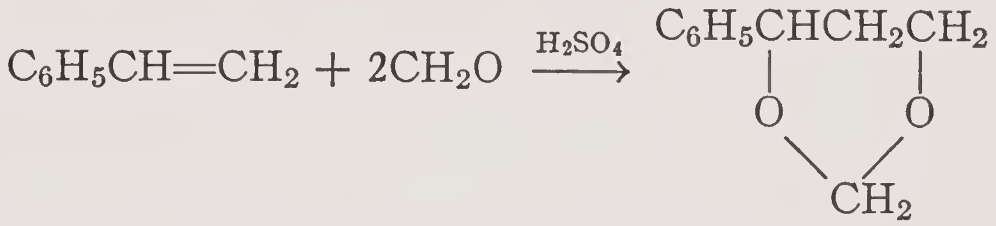
[6] Katoh, *Science Repts. Tokyo Bunrika Daigaku*, **2**, 257 (1935).

[7] Ishikawa and Tukeuchi, *Science Repts. Tokyo Bunrika Daigaku*, **A3**, 231 (1939).

[8] Oglialoro, *Gazz. chim. ital.*, **8**, 429 (1887).
[9] Bakunin, *Gazz. chim. ital.*, **31 II**, 77 (1901).
[10] Posner, *J. prakt. Chem.*, [2] **82**, 437 (1910).
[11] Johnson, in Adams, *Organic Reactions*, Vol. 1, p. 252, John Wiley & Sons, 1942.
[12] Buckles and Hausman, *J. Am. Chem. Soc.*, **70**, 415 (1948).
[13] Buckles, *J. Chem. Educ.*, **27**, 210 (1950).

4-PHENYL-*m*-DIOXANE

(*m*-Dioxane, 4-phenyl-)



Submitted by R. L. Shriner and Philip R. Ruby.[1]
Checked by Richard T. Arnold, W. E. Parham, and John E. Franz.

1. Procedure

In a 2-l. round-bottomed flask, fitted with a reflux condenser and mechanical stirrer, are placed 675 g. (8.3 moles) of 37% formalin, 48 g. of sulfuric acid (sp. gr. 1.84), and 312 g. (3 moles) of styrene. The resulting mixture is gently refluxed and stirred for 7 hours. The mixture is cooled, and 500 ml. of benzene is stirred in. The layers are separated, and the aqueous layer is extracted with 500 ml. of benzene. The benzene solutions are combined and washed with two 750-ml. portions of water. The benzene is removed by distillation, and the residual liquid is fractionated under reduced pressure. At 2 mm. pressure a fore-run is collected separately, up to a temperature of 96° (Note 1); then the main fraction is collected at 96–103°/2 mm. The yield of 4-phenyl-*m*-dioxane amounts to 353–436 g. (71–88%): n_D^{20} 1.5300–1.5311; d_4^{20} 1.092–1.093 (Note 2).

2. Notes

1. The amount of fore-run and the yield depend on the efficiency of the fractionation. With a 7-cm. distilling head, a fore-

run of 75 g. boiling at 84–96°/2 mm. was collected, whereas with a heated Vigreux column (2 cm. by 35 cm.) the fore-run amounted to only 11 g. and the higher yields were obtained. The fore-run may be refractionated to obtain additional product. The checkers used a 2 cm. by 20 cm. column packed with stainless-steel helices, and collected their product (72–75% yield) over a 1° boiling range (94–95°/2 mm., n_D^{20} 1.5300).

2. This modification of the Prins[2] reaction has been applied to other olefins.[3] The aryl olefins give the best yields; see the tabulation.

ARYL OLEFIN	YIELD OF SUBSTITUTED *m*-DIOXANE, %
α-Methylstyrene	58
Propenylbenzene	66
Anethole	89
Isosafrole	84
1-(3′,4′-Dimethoxyphenyl)-1-propene	68
1-(*p*-Cumyl)-1-propene	96

3. Methods of Preparation

4-Phenyl-*m*-dioxane was obtained by Prins[2] by the reaction between styrene and formaldehyde in the presence of sulfuric acid. The correct structure was pointed out by Fourneau, Benoit, and Firmenich.[4] The above procedure is essentially that given by Shortridge[5] and by Beets[3] and mentioned in a patent.[6] Methylphenylcarbinol has been substituted for styrene.[3]

[1] State University of Iowa, Iowa City, Iowa.

[2] Prins, *Chem. Weekblad*, **14**, 932 (1917); **16**, 1072, 1510 (1919); *Proc. Acad. Sci. Amsterdam*, **22**, 51 (1919).

[3] Beets, *Rec. trav. chim.*, **70**, 20 (1951); Beets and Van Essen, *Rec. trav. chim.*, **70**, 25 (1951); Drukker and Beets, *Rec. trav. chim.*, **70**, 29 (1951).

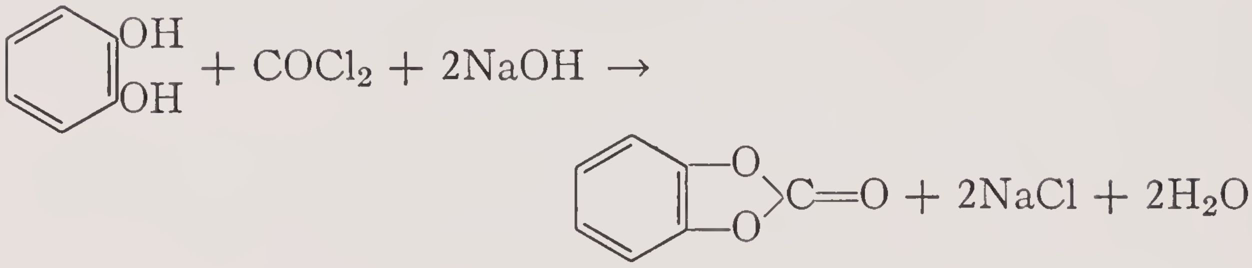
[4] Fourneau, Benoit, and Firmenich, *Bull. soc. chim. France*, **47**, 858 (1930).

[5] Shortridge, *J. Am. Chem. Soc.*, **70**, 873 (1948).

[6] Engel, U. S. pat. 2,417,548 [*C. A.*, **41**, 3493 (1947)].

o-PHENYLENE CARBONATE

(Carbonic acid, *o*-phenylene ester)



Submitted by R. S. Hanslick, W. F. Bruce, and A. Mascitti.[1]
Checked by Arthur C. Cope, Harris E. Petree, and Elmer R. Trumbull.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to toxic phosgene.

In a 5-l. three-necked flask, filled with nitrogen, 110 g. (1.0 mole) of recrystallized catechol (Note 1) is dissolved in 250 ml. of deaerated water (Note 2) containing 88 g. (2.2 moles) of sodium hydroxide. The flask is fitted with a gas inlet tube, a thermometer dipping into the liquid, and an efficient glass mechanical stirrer with a gas-tight rubber slip seal and is immersed in an ice-salt bath. A positive nitrogen pressure of about 1 cm. is maintained by attaching the inlet tube to a source of nitrogen through a line containing a T-tube dipping into mercury. A solution of 200–225 g. (2.0–2.3 moles) of commercial phosgene in 750 ml. of toluene is prepared at 0° by bubbling the gas into toluene in a tared flask (Note 3), and the solution is added to the flask in portions of about 50 ml. with good mechanical stirring over a period of 60 to 75 minutes. During the addition the temperature is maintained at 0–5° by periodic addition to the mixture of clean cracked ice, free from dirt and iron rust. After addition of the toluene solution of phosgene is completed, the mixture is stirred at 0–5° for 1 hour and then allowed to come to room temperature. The mixture is filtered with suction, and the solid is pressed on the funnel to remove as much water as possible. The aqueous portion of the filtrate is separated, and the solid on the funnel is added to the toluene in the filtrate and dissolved by warming. The warm toluene solution is filtered and distilled under reduced pressure (water aspirator) until the product begins to crystallize. The residue is warmed to redissolve the solid, and then chilled. The *o*-phenylene carbonate is collected on a suction filter and dried in a vacuum desiccator; the yield is 98–110 g., m.p. 119–120°.

Concentration of the filtrate yields a second crop of impure product, which is recrystallized from toluene and then melts at 119–120°. The combined yield of pure white *o*-phenylene carbonate from the first and second crops is 107–116 g. (79–86%).

2. Notes

1. Catechol obtained from the Koppers Company, Pittsburgh, Pennsylvania, was recrystallized from toluene.

2. Water that was deaerated by boiling was used, and an atmosphere of nitrogen essentially free from oxygen (such as the Seaford grade of the Air Reduction Company) was maintained, in order to prevent discoloration of the alkaline solution of catechol due to oxidation.

3. Phosgene from a commercial cylinder was used (Matheson Company or Ohio Chemical Company). For the preparation of a solution of phosgene in toluene see *Organic Syntheses*.[2]

3. Methods of Preparation

o-Phenylene carbonate has been prepared by the distillation of *o*-hydroxyphenyl ethyl carbonate,[3] and by the reaction of catechol with phosgene.[3,4]

[1] Research Laboratory, Wyeth Institute, Philadelphia, Pennsylvania.

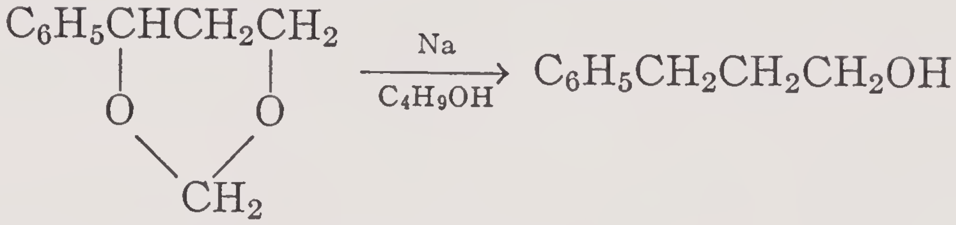
[2] *Org. Syntheses*, **23**, 13 (1943).

[3] Einhorn and Lindenberg, *Ann.*, **300**, 141 (1898).

[4] Nachfolger, Ger. pat. 72,806 [*Chem. Zentr.*, **65**, I, 805 (1894)].

3-PHENYL-1-PROPANOL

(1-Propanol, 3-phenyl-)



Submitted by R. L. Shriner and Philip R. Ruby.[1]
Checked by Richard T. Arnold, W. E. Parham, and Hans Wynberg.

1. Procedure

In a 5-l. round-bottomed flask, equipped with two reflux condensers and a mechanical stirrer (Note 1), are placed 800 g. (925 ml.) of dry toluene and 168 g. (7.3 gram atoms) of sodium metal. The toluene is heated to boiling, the sodium is melted, and the stirrer is started. The source of external heat is removed, and a solution of 328 g. (2 moles) of 4-phenyl-*m*-dioxane (p. 72) in 311 g. (4.2 moles) of 1-butanol (Note 2) is added through the top of one of the condensers. The vapors should reflux about halfway up the condensers; about 30 to 60 minutes is used for the addition (Note 3). The mixture is cooled to room temperature, and a solution of 100 ml. of concentrated sulfuric acid in 800 ml. of water is added slowly with stirring. After the water layer is separated and discarded, 500 ml. of water is again added to the organic layer. Dilute sulfuric acid (5%) is added with shaking until the water layer is neutral to litmus paper. After the water layer is separated and discarded, the toluene and 1-butanol are removed from the organic layer by distillation. The remaining liquid is fractionated under reduced pressure (Note 4) to give 224–227 g. (82.2–83.4%) of 3-phenyl-1-propanol, b.p. 95–97°/0.4 mm. or 113–115°/3 mm., n_D^{20} 1.5268–1.5269, d_4^{20} 1.004-1.008.

2. Notes

1. The condenser should have a large bore to prevent flooding. A wide-sweep stirrer such as a Hershberg stirrer should be used, and the stirring motor must be capable of operating under heavy loads. The checkers suggest that the minimum size for the stirrer be 8-mm. glass rod.

2. The butanol should be freshly dried and distilled.

3. The addition must be as rapid as possible. An additional 100 to 400 ml. of toluene may have to be added to facilitate stirring.

4. A heated 35-cm. Vigreux column is recommended, but a Claisen flask can be used if care is taken. If a Claisen flask is used, the distillation must not be carried out too rapidly, particularly near the end, at which point some of the residue tends to codistil.

3. Methods of Preparation

Ethyl cinnamate has been reduced to 3-phenyl-1-propanol with sodium and ethanol,[2-5] hydrogen and copper chromite,[6] and sodium and ammonia.[7] The alcohol has also been prepared by reduction of the glyceride of cinnamic acid with sodium and amyl alcohol; [8] by reduction of cinnamic acid with lithium aluminum hydride; [9] by reduction of cinnamoyl chloride with sodium borohydride; [10] and by reduction of ethyl dihydrocinnamate with sodium and ethanol.[2,11] Cinnamaldehyde has been reduced to 3-phenyl-1-propanol with hydrogen and palladium.[12,13] platinum,[14-16] or nickel,[17-20] nickel in alkaline solution (no hydrogen),[21] lithium aluminum hydride,[22] electrolysis at a mercury [23] or lead [24] electrode, and with an unmentioned catalyst.[25] Reduction of cinnamyl alcohol to 3-phenyl-1-propanol has been effected by use of sodium and ethanol,[26] sodium amalgam and water,[27,28] hydrogen and nickel [29] or palladium,[30] sodium and ammonia,[31] and lithium aluminum hydride.[32] Other syntheses have been brought about by reduction of ethyl α,β-epoxy-β-phenyldihydrocinnamate with sodium and amyl alcohol; [33] by reduction of ethyl benzoylacetate with hydrogen and copper chromite; [34] by reduction of acetonephenyllactic acid with hydrogen and copper chromite; [35] by reaction of ethyl alcohol with sodium benzylate; [36] and by reaction of benzylmagnesium chloride with a mixture of ethylene chlorohydrin and ethylmagnesium chloride.[37] The reduction of 4-phenyl-*m*-dioxane to give 3-phenyl-1-propanol, as described here, is based on the procedure of Beets,[38] who used sodium and diisobutylcarbinol. Other substituted *m*-dioxanes may also be converted to substituted 3-aryl-1-propanols by the same procedure.[39]

[1] State University of Iowa, Iowa City, Iowa.

[2] Bouveault and Blanc, *Compt. rend.*, **137**, 328 (1903); *Bull. soc. chim. France*, [3] **31**, 1209 (1904).

[3] Shorygin, Bogacheva, and Shepeleva, *Khim. Referat. Zhur.*, **1940**, 114 [*C. A.*, **36**, 3793 (1942)].

[4] Clutterbuck and Cohen, *J. Chem. Soc.*, **123**, 2509 (1923).

[5] Krushevskii and Gildburg, Russ. pat. 31,008 [*C. A.*, **28**, 3425 (1934)].

[6] Adkins and Folkers, *J. Am. Chem. Soc.*, **53**, 1095 (1931); Wojcik and Adkins, *J. Am. Chem. Soc.*, **55**, 4939 (1933).

[7] Chablay, *Compt. rend.*, **156**, 1022 (1913).

[8] Darzens, *Compt. rend.*, **205**, 682 (1937).

[9] Nystrom and Brown, *J. Am. Chem. Soc.*, **69**, 2548 (1947).

[10] Chaikin and Brown, *J. Am. Chem. Soc.*, **71**, 122 (1949).

[11] Burrows and Turner, *J. Chem. Soc.*, **119**, 428 (1921).

[12] Straus and Grindel, *Ann.*, **439**, 307 (1924).

[13] Endoh, *Rec. trav. chim.*, **44**, 869 (1925).

[14] Skita, *Ber.*, **48**, 1692 (1915).

[15] Tuley and Adams, *J. Am. Chem. Soc.*, **47**, 3063 (1925).

[16] Vavon, *Compt. rend.*, **154**, 361 (1912); *Ann. chim. et phys.*, [9] **1**, 166 (1914).

[17] Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).

[18] Braun and Kochendorfer, *Ber.*, **56**, 2175 (1923).

[19] Delepine and Hanegraaff, *Bull. soc. chim. France*, [5] **4**, 2087 (1937).

[20] Palfray, Sabetay, and Gauthier, *Compt. rend.*, **218**, 553 (1944).

[21] Papa, Schwenk, and Whitman, *J. Org. Chem.*, **7**, 587 (1942).

[22] Nystrom and Brown, *J. Am. Chem. Soc.*, **70**, 3738 (1948).

[23] Shima, *Mem. Coll. Sci. Kyoto Imp. Univ.*, **A12**, 70 (1929).

[24] Law, *J. Chem. Soc.*, **101**, 1030 (1912).

[25] Walter, Ger. pat. 296,507 [*C. A.*, **13**, 368 (1919)].

[26] Gray, *J. Chem. Soc.*, **127**, 1156 (1925).

[27] Hatton and Hodgkinson, *J. Chem. Soc.*, **39**, 319 (1881).

[28] Rugheimer, *Ann.*, **172**, 123 (1874).

[29] Tanaka, *Chem. Ztg.*, **48**, 25 (1924).

[30] Straus and Berkow, *Ann.*, **401**, 151 (1913).

[31] Chablay, *Compt. rend.*, **143**, 829 (1906); *Ann. chim. et phys.*, [9] **8**, 191 (1914).

[32] Hochstein and Brown, *J. Am. Chem. Soc.*, **70**, 3484 (1948).

[33] Verley, *Bull. soc. chim. France*, [4] **35**, 488 (1924).

[34] Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 3121 (1948).

[35] Oeda, *Bull. Chem. Soc. Japan*, **10**, 531 (1935).

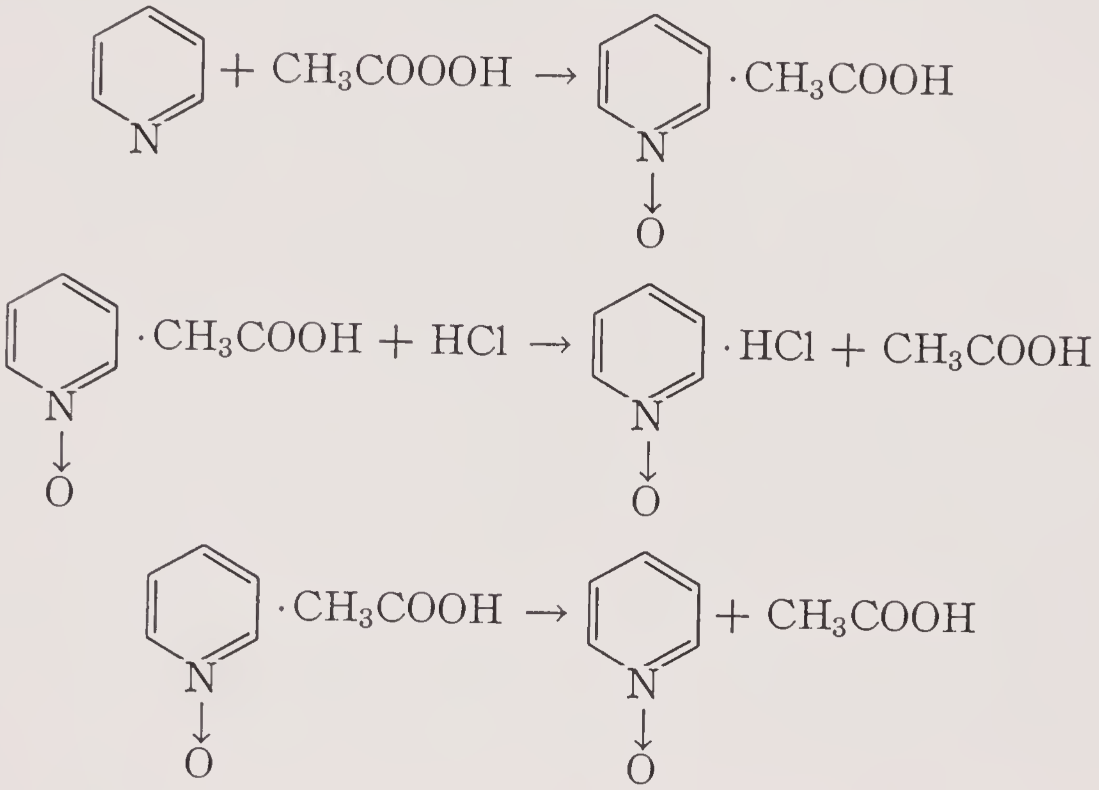
[36] Guerbet, *Compt. rend.*, **146**, 300 (1908); *Bull. soc. chim. France*, [4] **3**, 503 (1908).

[37] Conant and Kirner, *J. Am. Chem. Soc.*, **46**, 241 (1924).

[38] Beets, *Rec. trav. chim.*, **70**, 20 (1951).

[39] Beets and Van Essen, *Rec. trav. chim.*, **70**, 25 (1951); Drukker and Beets, *Rec. trav. chim.*, **70**, 29 (1951).

PYRIDINE-N-OXIDE



Submitted by Harry S. Mosher, Leslie Turner, and Allan Carlsmith.[1]
Checked by N. J. Leonard and E. D. Sutoris.

1. Procedure

In a 1-l. three-necked flask equipped with a stirrer (Note 1), a thermometer, and a dropping funnel is placed 110 g. (1.39 moles) of pyridine. The pyridine is stirred, and 250 ml. (285 g., 1.50 moles) of 40% peracetic acid (Note 2) is added at such a rate that the temperature reaches 85° and is maintained there. After the addition, which requires 50–60 minutes, the mixture is stirred until the temperature drops to 40°.

A. *Pyridine-N-oxide hydrochloride.* The acetate is converted to the hydrochloride by bubbling a slight excess over the theoretical amount (51 g.) of gaseous hydrogen chloride into the reaction mixture by way of a 7-mm. gas inlet tube which replaces the dropping funnel in the reaction flask. The acetic acid and excess peracetic acid are removed by warming on the steam bath under vacuum (Note 3). The residual pyridine-N-oxide hydrochloride is purified by heating under reflux for 30 minutes with 300 ml. of isopropyl alcohol, cooling to room temperature, and filtering. The colorless crystals are washed with 50 ml. of isopropyl alcohol followed by 50 ml. of ether. The yield is 139–152 g. (76–83%) (Note 4), m.p. 179.5–181°.

B. *Pyridine-N-oxide.* The acetic acid solution is evaporated on the steam bath under the pressure of a water aspirator, and the residue (180–190 g.) is distilled at a pressure of 1 mm. or less in an apparatus suitable for collecting a solid distillate (Note 5). The vacuum pump must be protected with a Dry Ice trap capable of holding about 60 ml. of acetic acid, which distils as the pyridine-N-oxide acetate dissociates at low pressure. Heat is provided by an oil bath, the temperature of which is not allowed to rise above 130° (Note 6). The product is collected at 100–105°/1 mm. (95–98°/0.5 mm.). The yield is 103–110 g. (78–83%) of colorless solid, m.p. 65–66° (sealed capillary). The base is deliquescent and must be stoppered immediately.

2. Notes

1. A convenient seal for stirring under vacuum (see Note 3) is made by running an 8-mm. glass rod, with propeller or paddle stirrer at the end, through the outside member of an 18/9 spherical joint which is inserted into a suitable rubber stopper. The inner member of the 18/9 spherical joint is then slipped over the stirrer and held in place with a piece of rubber tubing. This rotating seal may then be lubricated with a drop of oil. Alternatively, one may use a Tru-bore stirring system.

2. Becco peracetic acid (40%) was used. The composition and properties of this commercial preparation are described fully in *Bulletin* 4 of the Buffalo Electro-Chemical Company, Buffalo, New York. The manufacturer's recommendations for storing and handling should be followed. Experiments using propor-

tionate amounts of 10% or 20% peracetic acid in acetic acid were equally successful. The strength of the peracetic acid, as well as the progress of the reaction, can be determined iodimetrically.[2]

3. The vacuum evaporation proceeds much more smoothly and rapidly if the mixture is stirred mechanically during the process.

4. The submitters report that the same procedure is successful with four times the amounts given here. With the increased amounts, a water bath is used for cooling during the initial addition, which then requires about 45 minutes.

5. *Caution! Before distillation, absence of peroxide should be established by test with potassium iodide.*

The apparatus for distillation of solids in vacuum described in *Organic Syntheses*[3] is satisfactory, as is a combination of standard taper flasks, short column, and adaptors.

6. It is imperative that the pressure be maintained at 1 mm. or lower. Decomposition is usually extensive at higher pressures; however, the removal of the acetic acid may be initiated at 5–10 mm. pressure. The oil-bath temperature must not exceed 130° if decomposition is to be avoided. A fore-run of 15–20 g., b.p. 90–98°/0.5 mm., can be saved and redistilled in combination with similar cuts from successive runs. About 9–10 g. (7%) of additional crystalline pyridine-N-oxide is obtained per run in this manner.

3. Methods of Preparation

Pyridine-N-oxide has been prepared by oxidation of pyridine with perbenzoic acid,[4] with monoperphthalic acid,[5] with peracetic acid (hydrogen peroxide and acetic acid),[6,7] and with hydrogen peroxide and other carboxylic acids.[7]

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[1] Stanford University, Stanford, California.

[2] Smit, *Rec. trav. chim.*, **49**, 691 (1930).

[3] *Org. Syntheses*, **20**, 20 (1940).

[4] Meisenheimer, *Ber.*, **59**, 1848 (1926).

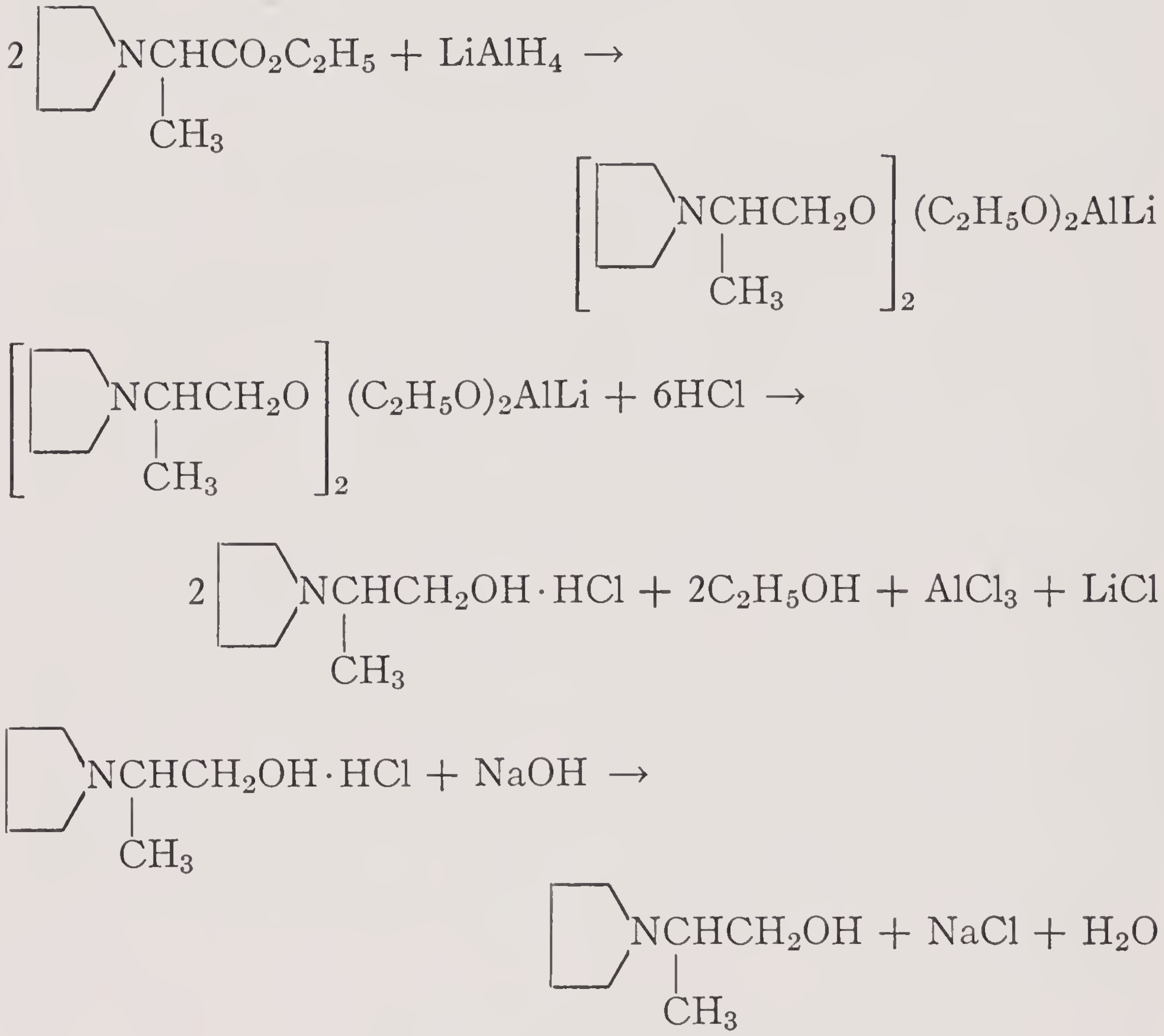
[5] Bobranski, Kochanska, and Kowalewska, *Ber.*, **71**, 2385 (1938).

[6] Ochiai, Ishikawa, and Zai-Ren, *J. Pharm. Soc. Japan*, **64**, 73 (1944) [*C. A.*, **45**, 8526*h* (1951)]; Hertog and Combe, *Rec. trav., chim.*, **70**, 581 (1951).

[7] Ochiai, Katada, and Hayashi, *J. Pharm. Soc. Japan*, **67**, 33 (1947) [*C. A.*, **45**, 9541*i* (1951)].

2-(1-PYRROLIDYL)-PROPANOL

(1–Pyrrolidineëthanol, β-methyl-)


2 NCHCO$_2$C$_2$H$_5$ + LiAlH$_4$ →
CH$_3$
[NCHCH$_2$O]$_2$ (C$_2$H$_5$O)$_2$AlLi
CH$_3$
[NCHCH$_2$O]$_2$ (C$_2$H$_5$O)$_2$AlLi + 6HCl →
CH$_3$
2 NCHCH$_2$OH·HCl + 2C$_2$H$_5$OH + AlCl$_3$ + LiCl
CH$_3$
NCHCH$_2$OH·HCl + NaOH →
CH$_3$
NCHCH$_2$OH + NaCl + H$_2$O
CH$_3$

Submitted by Robert Bruce Moffett.[1]
Checked by N. J. Leonard and S. Gelfand.

1. Procedure

A 2-l. three-necked round-bottomed flask in an electric heating mantle is fitted with a mercury-sealed Hershberg stirrer, a dropping funnel, and an efficient reflux condenser topped with a tube containing soda lime and calcium chloride. In this flask are placed 21.3 g. (0.56 mole) of pulverized lithium aluminum hydride (Note 1) and 300 ml. of dry ether. The mixture is heated under reflux until most of the hydride has dissolved. A solution of 157.3 g. (0.92 mole) of ethyl α-(1-pyrrolidyl)-propionate (p. 35) in 200 ml. of dry ether is then added slowly with vigorous stirring at such a rate that the solvent refluxes gently. When the addition is complete and the initial reaction subsides, the mixture is stirred at the reflux temperature an additional 30 minutes. The excess lithium aluminum hydride is decomposed by adding 50 ml. of ethyl acetate slowly with stirring. This is followed by 600 ml. of 6 *N* hydrochloric acid, added slowly with vigorous stirring.

The mixture is transferred to a separatory funnel. The water layer is separated, washed once with ether, and made strongly alkaline by the addition of 1 l. of 6 *N* sodium hydroxide (Note 2). The mixture is returned to the original 2-l. three-necked flask. An attachment for continuous ether extraction is placed in one of the side necks,[2] and 6-in. extension columns are placed in the other two necks. The stirrer is fitted through the center column and neck. Ether is added through the column attached to the side neck until the proper ether level is attained. A stopper is then placed on this column. The stirrer is run at such a rate that gentle swirling is accomplished without hindering the separation of the ether layer, and the continuous extraction with ether is continued until test with *p*H paper indicates that the ether coming over contains no more basic material. The ether solution of the product is thoroughly dried over anhydrous potassium carbonate (Note 3). The drying agent is removed by filtration, and the solvent by distillation at atmospheric pressure and finally at water-pump pressure. The residue is distilled at reduced pressure through a short fractionating column; b.p. 95–96°/20 mm. (109–110°/40 mm., 80°/11 mm.); n_D^{20} 1.4780; n_D^{25} 1.4758; d_4^{25} 0.9733. The yield is 95–106 g. (80–90%).

2. Notes

1. The hydride can be pulverized rapidly and safely by breaking the large pieces with a spatula, followed by careful crushing with a mortar and pestle. Caution must be observed because the solid may inflame on prolonged grinding or abrasion. The hydride dust is caustic and irritating.

2. At this point the mixture should be a mobile milky slurry. The submitter suggests that, if the mixture is too thick to extract, more water or base may be added.

3. Sufficient drying agent should be used so that no aqueous liquid phase appears.

3. Methods of Preparation

2-(1-Pyrrolidyl)-propanol has been prepared by the lithium aluminum hydride reduction of ethyl α-(1-pyrrolidyl)-propionate.[3]

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[1] The Upjohn Company, Kalamazoo, Michigan.

[2] *Org. Syntheses* Coll. Vol. **1**, 277 (1941).

[3] Moffett, *J. Org. Chem.*, **14**, 862 (1949).

STEARONE

(18-Pentatriacontanone)

$$2C_{17}H_{35}COOH + MgO \rightarrow (C_{17}H_{35}COO)_2Mg + H_2O$$

$$(C_{17}H_{35}COO)_2Mg \xrightarrow{340^\circ} C_{17}H_{35}COC_{17}H_{35} + MgO + CO_2$$

Submitted by A. G. Dobson and H. H. Hatt.[1]
Checked by R. L. Shriner and Philip R. Ruby

1. Procedure

In a 1-l. round-bottomed flask, fitted with a heated reflux condenser maintained at 100–110° (Note 1), are placed 44 g. of stearic acid (Note 2) and 20 g. (0.5 mole) of magnesium oxide (Note 3). The flask is immersed in a Wood's metal bath heated at 335–340° (Note 4). After the reaction has proceeded for 1 hour, 10-g. portions of melted stearic are added down the condenser at 15-minute intervals until an additional 240 g. (284 g., 1 mole total) has been added (Note 5). The heating is continued until the total reaction time is 10 hours.

The reaction flask is removed from the metal bath and allowed to cool to about 100°, and the liquid contents are poured with stirring into 1 l. of 4 *N* sulfuric acid in a 3-l. beaker. This mixture is boiled with vigorous mechanical stirring until the frothing ceases (Note 6) and the upper layer is clear (about 2 hours). The lower aqueous layer is then siphoned off, and the upper layer is boiled for 1 hour with 1 l. of water. The water layer is separated, and the upper layer is boiled with 1 l. of a 5% sodium hydroxide solution for 1 hour with vigorous stirring. The ketone layer is then separated and boiled for 1 hour each with three successive 1 l. portions of hot water (Note 7) with good stirring.

The crude stearone is allowed to solidify and is then broken up and dried by pressing between filter paper. The crude yield is 230–240 g. (91–95%). The product melts at 84–86° and has an acid value of zero. It is purified by dissolving in 1200 ml. of a 2:1 mixture of benzene and absolute ethanol, filtering hot, and allowing to crystallize (Note 8). After a second crystallization from the same mixed solvents, the stearone is obtained as glistening white flakes, melting clear at 89–89.5° (shrinks at 87–88°). The yield is 204–220 g. (81–87%) (Note 9).

2. Notes

1. The condenser, attached to the flask by a ground-glass joint, is a Pyrex tube 50 cm. long and 20 mm. in internal diameter, wound with No. 26 Nichrome wire covered with asbestos paper. It is connected to a variable transformer and adjusted so as to maintain a temperature of 100–110°. A copper Liebig condenser heated by steam is also suitable provided that the inner tube has a diameter of about 20 mm.

2. The purity and melting point of the final product are dependent on the purity of the stearic acid. If Armour's Neo-Fat 1-65, m.p. 64–67° (90–95% stearic acid) is recrystallized first from 95% ethanol and then from acetone, a stearic acid melting from 67° to 68° results which yields a stearone with a melting point of 88–89° (shrinks at 86–88°).

In order to obtain stearone with the highest melting point, the checkers found it necessary to purify the above recrystallized stearic acid by converting it to the methyl ester and fractionating this ester under reduced pressure, using a 30-in. electrically heated packed fractionating column. The fraction boiling at 180–182°/4 mm., n_D^{40} 1.4364, is collected. The methyl stearate solidifies on cooling and melts at 38–39°. Saponification and acidification yielded white crystals of stearic acid melting clear at 69–69.3° (cor.).

Commercial "stearone" (Armour) is made from Neo-Fat 1-60 (which is approximately 75% stearic and 25% palmitic acid) and melts at 80–84°.

3. Merck's reagent-grade magnesium oxide is suitable. The submitters recommend 10 g. of catalyst, but this amount gave a stearone with m.p. 87–88°. The larger amount, 20 g., gave a product melting clear at 89–89.5°.

4. The temperature of the bath should not be allowed to rise above 345°. Decomposition products are formed which lower the melting point of the final product.

5. With the rate of addition of stearic acid given, the decomposition of magnesium stearate maintains an excess of magnesium oxide in the reaction mixture. Each addition of stearic acid should take 1 to 2 minutes. Thus frothing of the reaction mixture is held under control; a brisk evolution of steam with a little entrained stearic acid follows each addition but quickly subsides and is followed by a steady effervescence due to the liberation of carbon dioxide.

6. A little unchanged magnesium stearate may cause frothing at this stage, which may be controlled by the addition of a few drops of 2-octanol and by vigorous stirring, which hastens decomposition of the soap.

7. The removal of fatty acids from neutral higher aliphatic compounds requires vigorous stirring of the hot aqueous and organic phases.

8. The solubility of stearone falls rapidly with temperature; a hot jacketed funnel is used with gentle suction.

9. This is a general method for the preparation of higher aliphatic ketones. It has been found suitable for the preparation of ketones from fatty acids containing 12 to 20 carbon atoms.

3. Methods of Preparation

Stearone has been prepared by heating the alkaline earth salts of stearic acid,[2] by reaction of liquid stearic acid with iron,[3-5] with alumina,[6] with manganous oxide and carbonate,[7] or with magnesium.[8] It has been prepared by passing stearic acid vapor over various catalysts: manganous oxide,[9] thoria aerogel,[10] or manganous oxide with chromium sesquioxide.[9] The literature contains numerous preparations from stearic acid using almost any metal or alkaline-earth oxides.

Kino [11] studied the reaction of stearic acid with magnesium oxide, with alloys of magnesium, and many other metals, at high temperatures, and obtained stearone. The present method was developed from a recent reëxamination of this reaction.[12]

[1] Council for Scientific and Industrial Research, Melbourne, Australia.

[2] Heintz, *Jahresber. Chem.*, **8**, 515 (1855).

[3] Easterfield and Taylor, *J. Chem. Soc.*, **99**, 2298 (1911).

[4] Grün, Ulbrich, and Krczil, *Z. angew. Chem.*, **39**, 423 (1926).

[5] Piper, Chibnall, Hopkins, Pollard, Smith, and Williams, *Biochem. J.*, **25**, 2074 (1931).

[6] Kino and Kato, *Bull. Inst. Phys. Chem. Research* (*Tokyo*), **19**, 179 (1940).

[7] Kino, *J. Soc. Chem. Ind. Japan*, **41**, 91 (1938).

[8] Kino, *J. Soc. Chem. Ind. Japan*, **40**, 194 (1937).

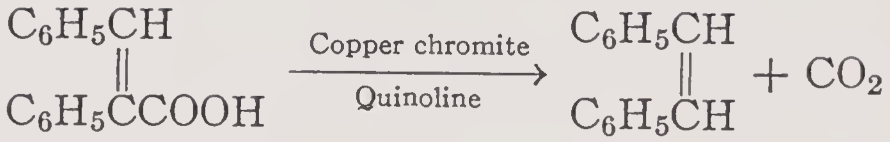
[9] Wortz, U. S. pat. 2,108,156 (1938) [*C. A.*, **32**, 2542 (1938)].

[10] Kistler, Swann, and Appel, *Ind. Eng. Chem.*, **26**, 388 (1934).

[11] Kino, *J. Soc. Chem. Ind. Japan*, **40**, 194, 235, 312, 437, 464 (1937); **41**, 91, 259 (1938); **42**, 188, 362 (1939).

[12] Curtis, Dobson, and Hatt, *J. Soc. Chem. Ind.*, **66**, 402 (1947).

cis-STILBENE



$$\begin{matrix} C_6H_5CH \\ \| \\ C_6H_5CCOOH \end{matrix} \xrightarrow[\text{Quinoline}]{\text{Copper chromite}} \begin{matrix} C_6H_5CH \\ \| \\ C_6H_5CH \end{matrix} + CO_2$$

Submitted by Robert E. Buckles and Norris G. Wheeler.[1]
Checked by T. L. Cairns and J. C. Lorenz.

1. Procedure

A 500-ml. three-necked flask is fitted with a reflux condenser and a thermometer, the bulb of which reaches far enough into the flask to be covered by the liquid. A solution of 46.0 g. (0.205 mole) of α-phenylcinnamic acid (p. 70) (Note 1) in 280 ml. (307 g., 2.38 moles) of quinoline (Note 2) is added to the flask along with 4.0 g. of copper chromite.[2] The reaction flask is heated by means of a mantle or an oil bath until the temperature of the reaction mixture reaches 210–220°. The mixture is kept within this temperature range for 1.25 hours. The solution is then cooled immediately and added to 960 ml. of 10% hydrochloric acid in order to dissolve the quinoline (Note 3). The product is extracted from this mixture with two 200-ml. portions of ether followed by a 100-ml. portion. The combined ether extracts are filtered to remove particles of catalyst, washed with 200 ml. of 10% sodium carbonate, and dried over anhydrous sodium sulfate. The dry solution is removed from the drying agent by filtration and heated on a steam bath to distil the ether. The residue is dissolved in a hexane fraction, b.p. 60–72° (Skellysolve B); the solution is cooled to 0° and filtered to remove *trans*-stilbene, if any. The hydrocarbon solvent is removed by distillation, and the *cis*-stilbene is distilled. The yield is 23–24 g. (62–65%), b.p. 133–136°/10 mm., 95–97°/1 mm.; n_D^{25} 1.6183–1.6193, n_D^{20} 1.6212–1.6218 (Note 4).

2. Notes

1. The isomer of α-phenylcinnamic acid of m.p. 172–173° is used.[3] The isomer of m.p. 137–139° yields *trans*-stilbene on decarboxylation.[4]

2. Practical quinoline containing about 10% of isoquinoline and quinaldine can be used. If the quinoline contains water, the desired temperature can be reached by distillation of a small amount of quinoline directly from the reaction mixture.

3. The quinoline can be recovered by neutralization of the aqueous solution, extraction of the quinoline into ether, and distillation of the dried (over barium oxide) ether extract.

4. The product obtained from this type of decarboxylation is reported to contain only about 5% of *trans*-stilbene.[5] A sample made according to the above directions can be treated with bromine in carbon tetrachloride at room temperature in the dark to give an 80–85% yield of the *dl*-dibromide which arises from *trans* addition to *cis*-stilbene. The *meso*-dibromide, which is very soluble and easily separated, is obtained only to the extent of 10% or less. Part of this latter product may arise from the action of bromine atoms on *cis*-stilbene rather than from *trans* addition to *trans*-stilbene. The *cis*-stilbene prepared by this method is readily and completely soluble in cold absolute ethanol. It freezes solid at about −5°. Its ultraviolet absorption coefficient (ε) is 1.10×10^4 at 274 mμ and 8.7×10^3 at 294 mμ, quite different from *trans*-stilbene.

3. Methods of Preparation

cis-Stilbene has been prepared by the partial hydrogenation of tolan,[6,7] by the electrolytic reduction of tolan,[8] by the reduction of tolan with a copper-zinc couple,[9] by the reduction of the low-melting isomer of α-bromostilbene with zinc dust in 90% alcohol,[10] by the illumination of *trans*-stilbene with ultraviolet light,[11] and by the decarboxylation of the high-melting isomer of α-phenylcinnamic acid in the presence of barium hydroxide.[4] The present method is based on that of Taylor and Crawford.[12]

[1] State University of Iowa, Iowa City, Iowa.

[2] *Org. Syntheses* Coll. Vol. **2**, 142 (1943).

[3] *Org. Syntheses*, **33**, 70 (1953).

[4] Stoermer and Voht, *Ann.*, **409**, 36 (1915).

[5] Weygand and Rettberg, *Ber.*, **73B**, 771 (1940).

[6] Kelber and Schwarz, *Ber.*, **45**, 1946 (1912).

[7] Ott and Schröter, *Ber.*, **60**, 624 (1927).

[8] Campbell and Young, *J. Am. Chem. Soc.*, **65**, 965 (1943).

[9] Straus, *Ann.*, **342**, 238 (1905).

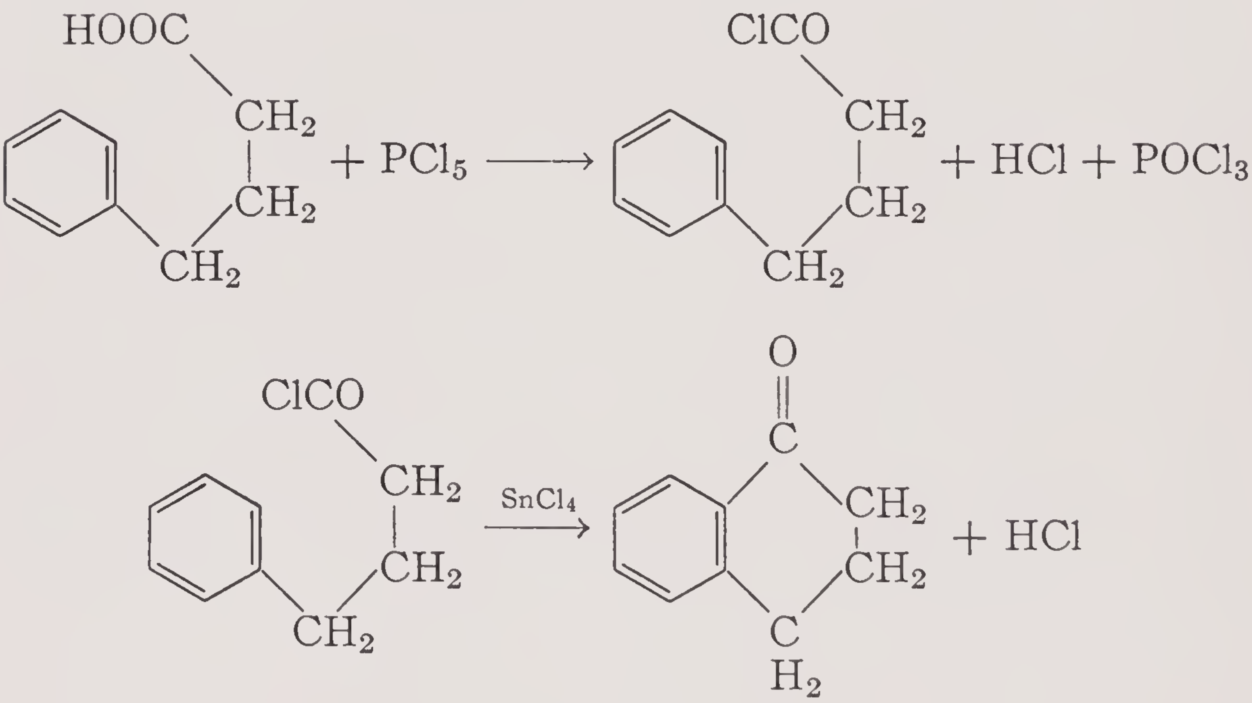
[10] Wislicenus and Jahrmarkt, *Chem. Zentr.*, **1901**, I, 463.

[11] Stoermer, *Ber.*, **42**, 4865 (1909).

[12] Taylor and Crawford, *J. Chem. Soc.*, **1934**, 1130.

α-TETRALONE

(1(2H)-Naphthalenone, 3,4-dihydro-)



Submitted by G. Dana Johnson.[1]
Checked by James Cason, William G. Dauben, Bradford H. Walker, and Charles E. Stehr.

1. Procedure

In a dry 2-l. three-necked round-bottomed flask, fitted with a gas-tight stirrer and a reflux condenser carrying at the top a calcium chloride drying tube connected to a gas-absorption trap (a good hood is preferable), are placed 98.5 g. (0.6 mole) of γ-phenylbutyric acid[2] and 200 ml. of dry thiophene-free benzene (Note 1). After the solution has been cooled, with stirring, for a few minutes in an ice bath, 125 g. (0.6 mole) of phosphorus pentachloride is added during 5 minutes (Note 2). After the ice bath is removed the contents of the flask are heated during 20 minutes (vigorous evolution of hydrogen chloride) to the boiling point by means of a water bath, and refluxing is continued for about 5 minutes. As stirring is continued the flask is cooled in an ice-salt bath until the internal temperature (Note 3) reaches about $-10°$. With continued efficient cooling, there is added during 30–40 minutes a solution of 150 ml. (1.34 moles) of anhydrous stannic chloride in 150 ml. of dry thiophene-free benzene (Note 1), as the temperature is maintained below 15°. The reaction is highly exothermic, and hydrogen chloride is rapidly evolved. Stirring is continued for 1 hour at 0–10°, at the end of which time the thermometer is replaced by the condenser and the complex is decomposed by careful addition of 300 g. of ice followed by 250 ml. of concentrated hydrochloric acid. This two-phase mixture is heated to reflux, with vigorous stirring, on a water bath for about 25 minutes or until hydrogen chloride is no longer evolved (Note 4).

The cooled reaction mixture is separated in a separatory funnel, and the aqueous phase is extracted with three 50-ml. portions of benzene. These extracts are combined with each other but kept separate from the original organic phase; each wash solution is used first with the original organic phase, then the extracts. The washes are 150 ml. of water (Note 4), 100 ml. of 10% sodium carbonate solution, 100 ml. of water, and finally 50 ml. of saturated sodium chloride solution (Note 5). Solvent is distilled from the combined extracts, and the residue is distilled at reduced pressure in a Claisen flask. The yield of α-tetralone, b.p. 135–137°/15 mm., n_D^{25} 1.5671–1.5672, is 75–80 g. (85–91%).

2. Notes

1. A total of 350 ml. of dry benzene is required. It may be dried by allowing it to stand for a few days with about 1 g. of

sodium wire, or by slowly distilling about 20% of a lot of benzene and cooling the residue with protection from atmospheric moisture by use of a calcium chloride tube.

2. It is convenient to weigh the phosphorus pentachloride in an Erlenmeyer flask which is then attached to a side neck of the three-necked flask by a 6-in. length of wide-bore thin-walled rubber tubing.

3. The condenser is replaced by a thermometer extending into the stirred liquid. The thermometer is inserted through a wide-bore T-tube whose side outlet is protected by a calcium chloride tube.

4. The stannic chloride complex is decomposed relatively slowly. Addition of 5–10 ml. of diethyl ether facilitates the decomposition. If the decomposition is not completed during the heating period, the wash with water gives a troublesome precipitation of stannic hydroxide. If this occurs the organic phase should either be heated for 30 minutes with, or allowed to stand overnight with, 100 ml. of 6 *N* hydrochloric acid.

5. The wash with saturated salt solution usually gives a clean separation and removes most of the water from the organic phase. No additional drying is necessary since the remaining water is removed by azeotropic distillation with benzene.

3. Methods of Preparation

Earlier methods of synthesis have been covered in *Organic Syntheses*.[3,4] The submitter experienced difficulty in preparing large quantities of sufficiently pure material by either of the above methods.

[1] Indiana University, Bloomington, Indiana.

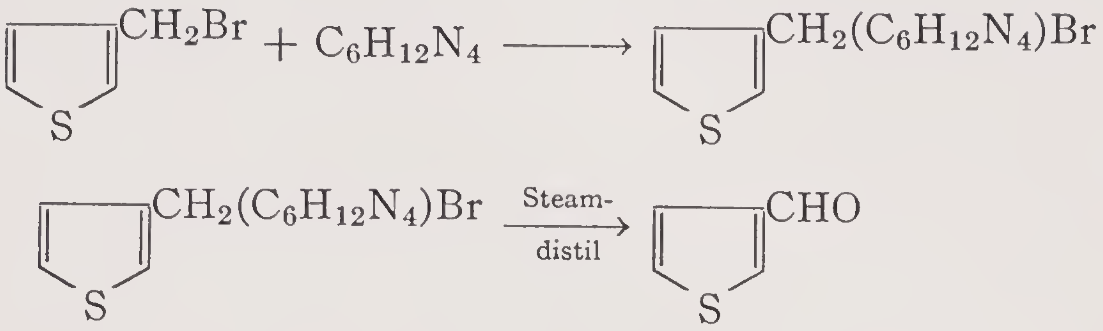
[2] *Org. Syntheses* Coll. Vol. **2**, 499 (1943).

[3] *Org. Syntheses* Coll. Vol. **2**, 569 (1943).

[4] *Org. Syntheses*, **20**, 94 (1940).

3-THENALDEHYDE

(3-Thiophenecarboxaldehyde)



Submitted by E. CAMPAIGNE, R. C. BOURGEOIS, and W. C. MCCARTHY.[1]
Checked by CHARLES C. PRICE and E. A. DUDLEY.

1. Procedure

Hexamethylene tetramine (77 g., 0.55 mole) is dissolved in 200 ml. of chloroform, and 88 g. (0.5 mole) of 3-thenyl bromide (p. 96) is added as rapidly as possible with shaking (Note 1). A reflux condenser is attached, and the mixture is refluxed over a steam bath for 30 minutes. After being cooled, the mixture of chloroform and crystalline product (Note 2) is poured into 250 ml. of water and stirred until all the salt dissolves. The chloroform layer is separated and washed twice with 125-ml. portions of water, and the combined water extracts are steam-distilled. When the distillate comes over clear (about 1 l. of distillate is usually collected), it is acidified with a little hydrochloric acid (Note 3) and extracted with three 100-ml. portions of ether. After drying over Drierite, the ether is evaporated, and the residue is distilled. 3-Thenaldehyde is collected at 72–78°/12 mm. or 195–199°/744 mm., $n_D^{20} = 1.5860$ (Note 4). The yield is 30–40 g. (54–71%).

2. Notes

1. The reaction mixture refluxes spontaneously, and it is necessary to be cautious in adding the reagents to prevent the chloroform from boiling over.

2. The crystalline hexamine salt may be isolated and recrystallized at this step. It softens at 120° and melts with decomposition at 150°.

3. The Sommelet procedure[2] yields a mixture of aldehyde and amines. Acidification removes the amines from the ether extract.

4. The checkers obtained the product, b.p. 80–81°/14 mm.

3. Methods of Preparation

3-Thenaldehyde has previously been prepared by Steinkopf and Schmitt[3] from 3-thienylmagnesium iodide and ethyl orthoformate in low yield. The first application of the method here described was reported by Campaigne and LeSuer.[4]

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[1] Indiana University, Bloomington, Indiana.

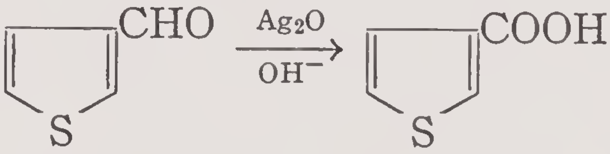
[2] Sommelet, *Compt. rend.*, **157**, 852 (1913).

[3] Steinkopf and Schmitt, *Ann.*, **533**, 264 (1938).

[4] Campaigne and LeSuer, *J. Am. Chem. Soc.*, **70**, 1555 (1948).

3-THENOIC ACID

(3-Thiophenecarboxylic acid)



Submitted by E. Campaigne and William M. LeSuer.[1]
Checked by Charles C. Price and E. A. Dudley.

1. Procedure

Silver oxide is prepared by adding a solution of 150 g. (0.89 mole) of silver nitrate in 300 ml. of water to a solution of 70 g. (1.75 moles) of sodium hydroxide in 300 ml. of water. Continuous shaking during the addition ensures complete reaction and results in a brown semisolid mixture. To this mixture, contained in a 1-l. flask which is cooled in an ice bath, is added 47.5 g. (0.425 mole) of 3-thenaldehyde (p. 93) in small portions with stirring.

The oxidation is complete in about 5 minutes after the last of the aldehyde has been added. The black silver suspension is removed by suction filtration (Note 1) and is washed with several portions of hot water. The cold combined filtrate and washings are acidified with concentrated hydrochloric acid, precipitating 49 g. of 3-thenoic acid, which melts at 136–137°. Concentration of the mother liquors gives another 3–4 g. of acid, making a total of 52–53 g. (95–97%). Recrystallization of this acid from water raises the melting point to 137–138°.

2. Notes

1. This silver dissolves readily in concentrated nitric acid and may be used over and over in oxidations.

3. Methods of Preparation

3-Thenoic acid has been prepared in low yield by oxidation of 3-methylthiophene with potassium permanganate,[2–4] dilute nitric acid, chromic acid, and hydrogen peroxide,[4] and by reductive dechlorination of chloro-3-thenoic acid.[4] Starting with 3-iodothiophene, which is difficult to obtain, good yields are obtained by the Grignard procedure [5] or with cuprous cyanide and potassium cyanide in a sealed tube.[6]

Oxidation of the aldehyde was not used earlier because of the difficulty of obtaining the aldehyde, which is now readily available by the Sommelet synthesis from 3-thenyl bromide. Campaigne and LeSuer [7] also used alkaline permanganate as the oxidizing agent, but the yields decreased to 40–60%. The present procedure gives an over-all yield from 3-methylthiophene of about 45%.

[1] Indiana University, Bloomington, Indiana.

[2] Muhlert, *Ber.*, **18**, 3003 (1885).

[3] Damsky, *Ber.*, **19**, 3282 (1886).

[4] Voerman, *Rec. trav. chim.*, **26**, 293 (1907).

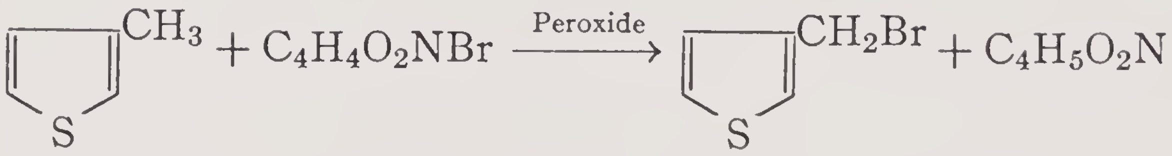
[5] Steinkopf and Schmitt, *Ann.*, **533**, 264 (1938).

[6] Rinkes, *Rec. trav. chim.*, **55**, 991 (1936).

[7] Campaigne and LeSuer, *J. Am. Chem. Soc.*, **70**, 1555 (1948).

3-THENYL BROMIDE

(Thiophene, 3-bromomethyl-)



Submitted by E. Campaigne and B. F. Tullar.[1]
Checked by Charles C. Price and E. A. Dudley.

1. Procedure

Caution! This preparation should be run in a well-ventilated hood.

A 5-l. three-necked flask (Note 1) is fitted with a stirrer, an efficient reflux condenser, and a wide-mouthed funnel with a 15-cm. water-cooled stem (Note 2). A solution of 220 g. (2.24 moles) of 3-methylthiophene (Note 3) and 4 g. of benzoyl peroxide in 700 ml. of dry benzene is brought to vigorous reflux in this flask, and a mixture of 356 g. (2 moles) of N-bromosuccinimide (Note 4) and 4 g. of benzoyl peroxide is added portionwise through the wide-mouthed funnel. The dry powder is added as rapidly as the violent foaming will permit (Note 5) and is worked down through the stem of the funnel with a stirring rod. Refluxing benzene washes the lower part of the funnel continuously. The total addition requires about 20 minutes. As soon as the foaming from the last addition of N-bromosuccinimide has subsided, the flask is cooled, first with a water bath and then an ice bath. The succinimide is filtered off and washed once with dry benzene.

The filtrate is immediately transferred to a distilling flask, and the benzene is removed at reduced pressure (Note 6). The residue is distilled at 1 mm., and the fraction boiling between 75° and 78° is collected (Note 7). The major portion boils at 76° and has n_D^{25} 1.6030. This procedure yields 250–280 g. (70–

80%) of a water-white product, which remains colorless for several days when stored over calcium carbonate in a refrigerator (Note 8).

2. Notes

1. The large volume of the flask is desirable to control foaming.

2. The checkers used a short, large-bore condenser.

3. Commercial 3-methylthiophene, formerly available from Socony-Vacuum Oil Company, was used. 3-Methylthiophene is now available from Winthrop-Stearns, Inc., Special Chemicals Division, New York 18, N. Y.

4. N-Bromosuccinimide can be prepared in an active state by two slight modifications of the Ziegler procedure.[2] A slight molar excess of sodium hydroxide is used, and the reaction mixture is stirred vigorously while the bromine, dissolved in an equal volume of carbon tetrachloride, is added rapidly. This produces a finely crystalline white product which is ready for use as soon as it is filtered from the water and carbon tetrachloride and thoroughly dried. The yields are generally improved by this procedure, and the N-bromosuccinimide is ready to use sooner than the product described by Ziegler et al.[2] Acetic acid is an excellent solvent for crystallization of crude *N*-bromosuccinimide.

5. Unless the reaction mixture is maintained at strong reflux during this addition, considerable nuclear bromination occurs with a corresponding decrease in 3-thenyl bromide yield.

6. If necessary to interrupt the procedure, the benzene solution of 3-thenyl bromide may be stored over calcium carbonate and distilled directly from the carbonate later. The addition of a little calcium carbonate before distillation avoids the formation of a difficultly removable tarry residue.

7. *Caution! This distillation should be carried out behind a safety shield.* Thenyl bromide is a powerful lachrymator, and some individuals may develop extensive irritation of the skin upon exposure to its vapors. The checkers observed boiling points of 78–82°/2 mm. and 80–85°/3 mm.

8. The product contains a trace of 2-bromo-3-methylthiophene, but no 2-bromo-3-thenyl bromide, and is sufficiently

pure for most purposes. Samples of 3-thenyl bromide have sometimes exploded without warning, leaving deposits of black resinous material. However, storage over calcium carbonate slows this acid-catalyzed reaction. The addition of a small amount of a tertiary amine likewise increases the stability.

3. Methods of Preparation

The only method of preparative interest is that described by Campaigne and LeSuer,[3] upon which the present method is based. This method has been applied by Dittmer et al.[4]

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[1] Indiana University, Bloomington, Indiana.

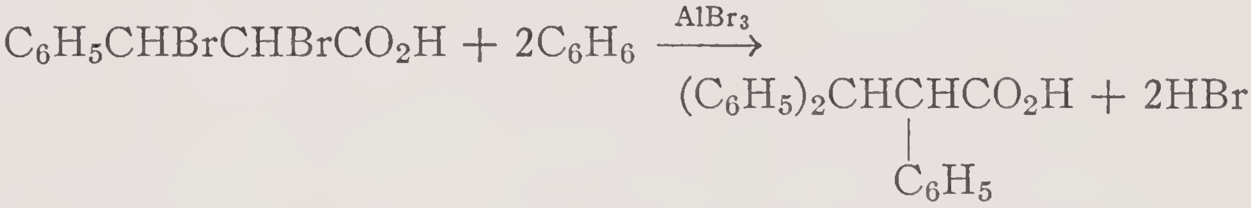
[2] Ziegler, Spath, Schaaf, Schumann, and Winkelmann, *Ann.*, **551**, 80 (1942).

[3] Campaigne and LeSuer, *J. Am. Chem. Soc.*, **70**, 1555 (1948).

[4] Dittmer, Martin, Herz, and Cristol, *J. Am. Chem. Soc.*, **71**, 1201 (1949).

α,β,β-TRIPHENYLPROPIONIC ACID

(Propionic acid, α,β,β-triphenyl-)



$$C_6H_5CHBrCHBrCO_2H + 2C_6H_6 \xrightarrow{AlBr_3} (C_6H_5)_2CH\underset{\substack{| \\ C_6H_5}}{C}HCO_2H + 2HBr$$

Submitted by C. P. Krimmel, L. E. Thielen, E. A. Brown, and W. J. Heidtke.[1]
Checked by William S. Johnson, A. L. Wilds, and J. S. Jellinek.

1. Procedure

A 5-l. three-necked flask is fitted with a mechanical rubber-sleeved stirrer, a dropping funnel, and a reflux condenser capped with a calcium chloride tube leading to a gas-absorption trap.[2] The system is flame-dried, and the flask is charged with 308 g. (1 mole) of dibromohydrocinnamic acid (Note 1) and 800 ml. of dried (by distillation) thiophene-free benzene. While the dibromohydrocinnamic acid is maintained in suspension by stirring (Note 2), a freshly prepared solution of 294 g. (1.1 moles) of anhydrous aluminum bromide (Note 3) in 400 ml. of anhydrous thiophene-free benzene is added from the dropping funnel over a period of 30 minutes. The clear orange-to-red solution is then heated under reflux with stirring for 4 hours.

The mixture is cooled to room temperature and maintained there with the aid of a cooling bath while 500 ml. of concentrated hydrochloric acid is added slowly from the dropping funnel. The mixture should be stirred vigorously during this addition, which requires about 30 minutes and is accompanied by copious evolution of hydrogen bromide (Note 4) and separation of the α,β,β-triphenylpropionic acid as a thick white slurry. Stirring is continued for an additional 30 minutes, 2 l. of water is added, and the product is separated by suction filtration. The waxy filter cake is washed with two 250-ml. portions of water, then dried overnight at room temperature and finally at 75° (Note 5). The crude, almost colorless α,β,β-triphenylpropionic acid amounts to 287–302 g. (95–100% yield), m.p. 215–218°. Recrystallization by dissolution in 3 l. of isopropyl alcohol (Note 6), followed by concentration of the filtered solution to 1.5 l. before cooling, yields 200–236 g. (66–78%) of colorless needles, m.p. 220–221°.

2. Notes

1. Dibromohydrocinnamic acid is conveniently prepared by the method of Reimer.[3] The checkers employed the following procedure. To a gently boiling solution of 296 g. (2 moles) of cinnamic acid in 2 l. of c.p. carbon tetrachloride contained in a 5-l. three-necked flask fitted with a reflux condenser, a dropping funnel, and a mechanical stirrer is added slowly (1.5 hours) with stirring 320 g. (2 moles) of bromine dissolved in 200 ml. of carbon tetrachloride. After 25–50% of the bromine is added, the dibromohydrocinnamic acid begins to precipitate with evolution of heat. Stirring and heating are continued for an additional 30 minutes after all the bromine is added. The mixture is cooled to room temperature; the product is separated by suction filtration and is washed with a small amount of cold carbon tetrachloride.

The air-dried product amounts to 558–580 g. (91–94% yield) of colorless crystals, m.p. 197–198° to 202–204°.

2. If a solution instead of suspension is used, troublesome gel formation may occur during the aluminum bromide addition.

3. Colorless, crystalline, anhydrous aluminum bromide supplied by the Westvaco Chemical Division, Food Machinery and Chemical Corporation, New York, New York, was used. When dissolved in dry benzene at room temperature with mechanical stirring, a perfectly clear yellow solution results, if the reagents are of high purity.

4. If stirring is not sufficiently vigorous or if the temperature is too low, the evolution of hydrogen bromide may be delayed and then may begin abruptly and be difficult to control.

5. If the wet product is introduced directly into the drying oven it may darken slightly.

6. If the solution is appreciably colored it may be treated with decolorizing carbon at this point. Toluene or dilute ethanol may also be used for the recrystallization, but these solvents are less satisfactory.

3. Methods of Preparation

α,β,β-Triphenylpropionic acid has been prepared by the alkaline hydrolysis of the addition product of phenylmagnesium bromide and methyl α-phenylcinnamate;[4] by the reaction of α-phenylcinnamic acid with benzene in the presence of aluminum chloride;[5] and by the reaction of dibromohydrocinnamic acid with benzene in the presence of aluminum bromide or ferric chloride.[6] The procedure described here is a modification of the method of Earl and Wilson.[6]

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[1] G. D. Searle and Company, Chicago, Illinois.

[2] *Org. Syntheses* Coll. Vol. **2**, 4 (1943).

[3] Reimer, *J. Am. Chem. Soc.*, **64**, 2510 (1942).

[4] Kohler and Heritage, *Am. Chem. J.*, **33**, 156 (1905).

[5] Eijkman, *Chem. Weekblad*, **5**, 655 (1908) (*Chem. Zentr.*, **1908**, II, 1100).

[6] Earl and Wilson, *J. Proc. Roy. Soc. N. S. Wales*, **65**, 178 (1932) [*C. A.*, **26**, 2976 (1932)].

SUBJECT INDEX

(This cumulative index comprises material from Volumes 30, 31, 32, and 33; for previous volumes see Collective Volumes 1 and 2 and Volume 29.)

Names in small capital letters refer to the titles of individual preparations. A number in ordinary bold-face type denotes the volume. A page number in bold-face italics indicates that the detailed preparative directions are given or referred to; entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations. For example, Allylbenzene, **31**, 85, ***86***, indicates that allylbenzene is mentioned on page 85, and that directions for its preparation are given on page 86, of Volume 31.

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